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Henry Ford Health System Publication List – November 2016

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health System personnel. Searches were conducted in PubMed, Embase, Web of Science, and Google Scholar during the beginning of December, and then imported into EndNote for formatting. There are 144 unique citations listed this month. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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Behavioral Health Services

Ahmedani BK, **Belville-Robertson T**, Hirsch A, and **Jurayj A**. An online mental health and wellness intervention supplementing standard care of depression and anxiety *Arch Psychiatr Nurs* 2016; 30(6):666-670. PMID: 27888957. Full Text

Henry Ford Health System, Center for Health Policy and Health Services Research, Detroit, MI; Henry Ford Health System, Behavioral Health Services, Detroit, MI. Electronic address: bahmeda1@hfhs.org.
Henry Ford Health System, Behavioral Health Services, Detroit, MI.
MyStrength, Incorporated(c), Greenwood Village, CO.
Henry Ford Health System, Center for Health Policy and Health Services Research, Detroit, MI.

Online interventions offer benefits, but often have not been tested in studies. The aim was to study feasibility, acceptability, and preliminary effectiveness of an online intervention supplementing standard care of depression and anxiety. The study was conducted within a large healthcare system. Three primary care and four behavioral health providers recruited 96 participants. Overall, 91% (n=87) agreed to participate, while 43% (n=41) completed registration and 27% (n=26) logged into the intervention multiple times. Participants referred by behavioral health demonstrated greater involvement. Reductions in depression and anxiety were observed. Most providers were satisfied with the intervention. This study supports future research.

Behavioral Health Services

Henein F, **Prabhakar D**, **Peterson EL**, **Williams LK**, and **Ahmedani BK**. A prospective study of antidepressant adherence and suicidal ideation among adults *Prim Care Companion CNS Disord* 2016; 18(6)PMID: 27907275. Article Request Form

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Cardiology

Ades PA, **Keteyian SJ**, Wright JS, Hamm LF, Lui K, Newlin K, Shepard DS, and Thomas RJ. Increasing cardiac rehabilitation participation from 20% to 70%: A road map from the million hearts cardiac rehabilitation collaborative *Mayo Clin Proc* 2016;PMID: 27855953. Full Text

Cardiac Rehabilitation and Prevention Program, University of Vermont College of Medicine, Burlington, VT. Electronic address: Philip.ades@uvmhealth.org.
Preventive Cardiology, Henry Ford Hospital, Detroit, MI.
Million Hearts, Centers for Disease Control and Prevention, Atlanta, GA.
Clinical Exercise Physiology Program, Department of Exercise and Nutrition Sciences, George Washington University, Washington, DC.

GRQ, LLC, Vienna, VA.
Cardiac and Pulmonary Rehabilitation, Sutter Roseville Medical Center, Roseville, CA.
Heller School for Social Policy and Management, Brandeis University, Waltham, MA.
Cardiac Rehabilitation Program, Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN.

The primary aim of the Million Hearts initiative is to prevent 1 million cardiovascular events over 5 years. Concordant with the Million Hearts' focus on achieving more than 70% performance in the "ABCS" of aspirin for those at risk, blood pressure control, cholesterol management, and smoking cessation, we outline the cardiovascular events that would be prevented and a road map to achieve more than 70% participation in cardiac rehabilitation (CR)/secondary prevention programs by the year 2022. Cardiac rehabilitation is a class Ia recommendation of the American Heart Association and the American College of Cardiology after myocardial infarction or coronary revascularization, promotes the ABCS along with lifestyle counseling and exercise, and is associated with decreased total mortality, cardiac mortality, and rehospitalizations. However, current participation rates for CR in the United States generally range from only 20% to 30%. This road map focuses on interventions, such as electronic medical record-based prompts and staffing liaisons that increase referrals of appropriate patients to CR, increase enrollment of appropriate individuals into CR, and increase adherence to longer-term CR. We also calculate that increasing CR participation from 20% to 70% would save 25,000 lives and prevent 180,000 hospitalizations annually in the United States.

Cardiology

Beri N, Marston NA, Daniels LB, **Nowak RM**, Schreiber D, Mueller C, Jaffe A, Diercks DB, Wettersten N, DeFilippi C, Peacock WF, Limkakeng AT, Anand I, McCord J, **Hollander JE**, Wu AH, Apple FS, Nagurney JT, Berardi C, Cannon CM, Clopton P, Neath SX, Christenson RH, Hogan C, Vilke G, and Maisel A. Necessity of hospitalization and stress testing in low risk chest pain patients *Am J Emerg Med* 2016;PMID: 27847253. Full Text

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Department of Emergency Medicine, Duke University, Durham, NC, United States.
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Department of Pathology, Hennepin County Medical Center and University of Minnesota, Minneapolis, United States.
Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA, United States.
School of Medicine, "La Sapienza" University of Rome, Rome, Italy.
Department of Emergency Medicine, University of Kansas, Kansas City, KS, United States.
Statistics, Veterans Affairs Medical Center, San Diego, CA, United States.
Department of Emergency Medicine, University of California, San Diego, La Jolla, CA, United States.
Department of Pathology, University of Maryland, Baltimore, MD, United States.
Department of Surgery, Virginia Commonwealth University, Richmond, VA, United States.

BACKGROUND: Copeptin is a marker of endogenous stress including early myocardial infarction(MI) and has value in early rule out of MI when used with cardiac troponin I(cTnI). OBJECTIVES: The goal of this study was to demonstrate that patients with a normal electrocardiogram and cTnI<0.040mug/l and copeptin<14pmol/l at presentation and after 2 h may be candidates for early discharge with outpatient follow-up potentially including stress testing. METHODS: This study uses data from the CHOPIN trial which enrolled 2071 patients with acute chest pain. Of those, 475 patients with normal electrocardiogram and normal cTnI(<0.040mug/l) and copeptin<14pmol/l at presentation and after 2 h were considered "low risk" and selected for further analysis. RESULTS: None of the 475 "low risk" patients were diagnosed with MI during the 180day follow-up period (including presentation). The negative predictive value of this strategy was 100% (95% confidence interval(CI):99.2%-100.0%). Furthermore no one died during follow up. 287 (60.4%) patients in the low risk group were hospitalized. In the "low risk" group, the only

difference in outcomes (MI, death, revascularization, cardiac rehospitalization) was those hospitalized underwent revascularization more often (6.3%[95%CI:3.8%-9.7%] versus 0.5%[95%CI:0.0%-2.9%], p=.002). The hospitalized patients were tested significantly more via stress testing or angiogram (68.6%[95%CI:62.9%-74.0%] vs 22.9%[95%CI:17.1%-29.6%], p<.001). Those tested had less cardiac rehospitalizations during follow-up (1.7% vs 5.1%, p=.040). CONCLUSIONS: In conclusion, patients with a normal electrocardiogram, troponin and copeptin at presentation and after 2 h are at low risk for MI and death over 180days. These low risk patients may be candidates for early outpatient testing and cardiology follow-up thereby reducing hospitalization.

Cardiology

Garcia S, Chadi Alraies M, Karatasakis A, Yannopoulos D, Karmpaliotis D, **Alaswad K**, Jaffer FA, Yeh RW, Patel MP, Bahadorani J, Karacsonyi J, Kalsaria P, Danek B, Banerjee S, and Brilakis ES. Coronary artery spatial distribution of chronic total occlusions: Insights from a large US registry *Catheter Cardiovasc Interv* 2016;PMID: 27860111. Full Text

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VA North Texas Health Care System and University of Texas Southwestern Medical Center, Dallas, Texas.
Columbia University, New York, New York.
Henry Ford Health System, Edith and Benson Ford Heart and Vascular Institute, Detroit, Michigan.
Massachusetts General Hospital, Boston, Massachusetts.
UC San Diego Medical Center, San Diego, California.

OBJECTIVE: To assess the spatial distribution of chronic total occlusions (CTOs) within the coronary arteries and describe procedural strategies and outcomes during CTO percutaneous coronary intervention (PCI). BACKGROUND: Acute occlusions due to plaque rupture tend to cluster within the proximal third of the coronary artery. METHODS: We examined the clinical and procedural characteristics of 1,348 patients according to lesion location within the coronary tree. RESULTS: A total of 1,369 lesions in 1,348 patients (mean age 66 +/- 10 years, 85% male) were included. CTO PCI of proximal segments (n = 633, 46%) was more common than of mid (n = 557, 41%) and distal segments (n = 179, 13%). Patients undergoing CTO PCI of proximal segments were more likely to be smokers (P < 0.01), have prior coronary artery bypass graft surgery (P = 0.03) and lower ejection fraction (P = 0.04). CTOs occurring in proximal segments had longer length (P <0.01), proximal cap ambiguity (P < 0.01), and moderate/severe calcification (P < 0.01) compared to mid or distally located CTOs. Interventional collaterals were more often present in CTO PCI of proximal segments (64%, 53%, 56%, P < 0.01) consistent with the higher use of retrograde approach (47%, 33%, 37%, P < 0.01) relative to antegrade wire escalation (67%, 82%, 82%, P < 0.01). Procedural complexity was higher in CTO PCI of proximal segments (vs. mid and distal): contrast volume= 275 ml (200-375), 260 ml (200-350), 250 ml (175-350), P = 0.01; fluoroscopy time 53 minutes (32-83), 39 minutes (24-65), 40 minutes (22-72), P < 0.01. However, procedural success (87%, 90%, 85%, P = 0.1), technical success (89%, 91%, 88%, P = 0.24), and complications rates (2.8%, 2.5%, 2.2%, P = 0.88) were not different. CONCLUSIONS: The most common target vessel location for CTO PCI is the proximal coronary segment. PCI of proximal occlusions is associated with adverse clinical and angiographic characteristics and often requires use of the retrograde approach, but can be accomplished with high procedural and technical success and low complication rates. (c) 2016 Wiley Periodicals, Inc.

Cardiology

Hudson M. PCI with drug-eluting stents reduced revascularizations, but not mortality or MI, compared with bare-metal stents *Ann Intern Med* 2016; 165(10):Jc52. PMID: 27842389. Full Text

Henry Ford HospitalDetroit, Michigan, USA.

Cardiology

Kelly JP, Dunning A, Schulte PJ, Fiuzat M, Leifer ES, Fleg JL, Cooper LS, **Keteyian SJ**, Kitzman DW, Pina IL, Kraus WE, Whellan DJ, O'Connor CM, and Mentz RJ. Statins and exercise training response in heart failure patients: Insights from hf-action *JACC Heart Fail* 2016; 4(8):617-624. PMID: 27395348. Full Text

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Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina; Duke Clinical Research Institute, Durham, North Carolina.
Division of Cardiovascular Science, National Heart, Lung, and Blood Institute, Bethesda, Maryland.

Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan.
Section of Cardiology, Department of Internal Medicine, Wake Forest University, Winston-Salem, North Carolina.
Division of Cardiology, Department of Medicine, Albert Einstein College of Medicine, New York, New York.
Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina; Duke Molecular Physiology Institute, Durham, North Carolina.
Division of Cardiology, Thomas Jefferson University, Philadelphia, Pennsylvania.

OBJECTIVES: The aim of this study was to assess for a treatment interaction between statin use and exercise training (ET) response. BACKGROUND: Recent data suggest that statins may attenuate ET response, but limited data exist in patients with heart failure (HF). METHODS: HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training) was a randomized trial of 2,331 patients with chronic HF with ejection fraction </=35% who were randomized to usual care with or without ET. We evaluated whether there was a treatment interaction between statins and ET response for the change in quality of life and aerobic capacity (peak oxygen consumption and 6-min walk distance) from baseline to 3 months. We also assessed for a treatment interaction among atorvastatin, simvastatin, and pravastatin and change in these endpoints with ET. Multiple linear regression analyses were performed for each endpoint, adjusting for baseline covariates. RESULTS: Of 2,331 patients in the HF-ACTION trial, 1,353 (58%) were prescribed statins at baseline. Patients treated with statins were more likely to be older men with ischemic HF etiology but had similar use of renin angiotensin system blockers and beta-blockers. There was no evidence of a treatment interaction between statin use and ET on changes in quality of life or exercise capacity, nor was there evidence of differential association between statin type and ET response for these endpoints (all p values >0.05). CONCLUSIONS: In a large chronic HF cohort, there was no evidence of a treatment interaction between statin use and short-term change in aerobic capacity and quality of life with ET. These findings contrast with recent reports of an attenuation in ET response with statins in a different population, highlighting the need for future prospective studies. (Exercise Training Program to Improve Clinical Outcomes in Individuals With Congestive Heart Failure; NCT00047437).

Cardiology

McDonagh JR, Seth M, LaLonde TA, **Khandewal AK**, Wohns DH, Dixon SR, and Gurm HS. Radial pci and the obesity paradox: Insights from blue cross blue shield of michigan cardiovascular consortium (bmc2) *Catheter Cardiovasc Interv* 2016; 87(2):211-219. PMID: 26010906. Full Text

Division of Cardiovascular Medicine, University of Michigan Medical Center, Ann Arbor, Michigan.
Blue Cross Blue Shield of Michigan Cardiovascular Consortium, University of Michigan Medical Center, Ann Arbor, Michigan.
Division of Cardiology, St. John Providence Health System, Wayne State University, Detroit, Michigan.
Division of Cardiology, Henry Ford Health System, Detroit, Michigan.
Spectrum Health, Grand Rapids, Michigan.
Department of Cardiovascular Medicine, Beaumont Hospital, Royal Oak, Michigan.

OBJECTIVE: To examine if transradial approach (TRA) negates the increased risk associated with femoral access in lean and morbidly obese patients undergoing percutaneous coronary intervention (PCI). BACKGROUND: Patients at extremes of body mass are at increased risk of bleeding after PCI. TRA has been associated with lower overall rates of bleeding compared to femoral approach. METHODS AND RESULTS: We studied patients undergoing emergent and elective PCI from 2010 to 2012 across 47 hospitals in Michigan who participate in the Blue Cross Blue Shield of Michigan Cardiovascular Consortium PCI registry. The primary outcomes were the incidences of bleeding and postprocedure transfusion. Propensity matching (PM) was used to adjust for nonrandomized use of TRA. TRA was used in 10,235 procedures. In PM analyses, use of TRA was associated with a reduction in bleeding (0.80 vs. 1.9%, odds ratio [OR] = 0.41, 95% confidence interval [CI] = 0.32-0.54, P < 0.001) and need for transfusion (1.4 vs. 2.5%, OR = 0.56, 95% CI = 0.45-0.69, P < 0.001) compared with femoral access. The absolute difference in bleeding and transfusion associated with TRA was largest in patients with lean body mass (BMI < 25 kg/m(2)) and morbid obesity (BMI >/= 40 kg/m(2)): Lean patients undergoing TRA had a rate of bleeding of 1.2 versus 2.8% for femoral access (OR = 0.43, 95% CI = 0.24-0.77, P = 0.002); and rate of transfusion of 2.4 versus 3.9% (OR = 0.61, 95% CI = 0.40-0.94, P = 0.019). The morbidly obese had a rate of bleeding of 0.8% for TRA versus 2.4% for femoral access (OR = 0.33, 95% CI = 0.44-0.72, P = 0.004); and rate of transfusion of 1.7 versus 3.0%, (OR = 0.55, 95% CI = 0.30-1.0, P = 0.051). CONCLUSIONS: Compared with the femoral approach, TRA is associated with a reduction in bleeding across all patients undergoing PCI and the absolute benefit was greatest in those with extremely low or high BMI.

Cardiology

Reddy VY, Gibson DN, Kar S, **O'Neill W**, Doshi SK, Horton RP, Buchbinder M, Gordon NT, and Holmes DR. Post-FDA Approval, Initial US clinical experience with watchman left atrial appendage closure for stroke prevention in atrial fibrillation *J Am Coll Cardiol* 2016;PMID: 27816552. Full Text

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Texas Cardiac Arrhythmia Institute, Austin, TX.
Foundation for Cardiovascular Medicine, La Jolla, CA.
Boston Scientific Corporation, St. Paul, MN.
Department of Cardiology, Mayo Clinic, Rochester, MN.

BACKGROUND: Left atrial appendage closure (LAAC) using the Watchman device was FDA-approved as a stroke prevention alternative to warfarin for patients with non-valvular atrial fibrillation. However, clinical decision-making is confounded by the fact that while LAAC avoids the anticoagulant-related lifetime risk of bleeding, implantation is associated with up-front complications. Thus, enthusiasm for LAAC as a treatment option has been appropriately tempered, particularly as the therapy is introduced beyond the clinical trial sites into general clinical practice. OBJECTIVES: To evaluate the acute procedural performance and complication rates for all Watchman cases performed in the US since FDA approval. METHODS: In the absence of a formal national clinical registry since regulatory approval in March 2015, we obtained procedural data on Watchman implantation procedures. Briefly, every LAAC procedure requires the presence of a manufacturer clinical specialist, and procedural parameter and peri-procedural complication data are collected using a standardized process and forms. RESULTS: In 3,822 consecutive cases, implantation was successful in 3,653 (95.6%) with a median procedure time of 50 min (range 10, 210); implanting physicians performing these procedures (n=382) included 71% new, non-clinical trial implanters, performing 50% of the procedures. Procedural complication rates included: 39 pericardial tamponades (1.02%; 24 treated percutaneously, 12 surgically and 3 fatal), three procedure-related strokes (0.078%), 9 device embolizations (0.24%; 6 requiring surgical removal), and 3 procedure-related deaths (0.078%). CONCLUSIONS: Despite a large fraction of previously-inexperienced operators, in the real-world post-FDA approval experience of Watchman LAAC, procedural success was high and complication rates low.

Cardiology

Wang DD, **Eng M**, **Kupsky D**, **Myers E**, **Forbes M**, **Rahman M**, **Zaidan M**, **Parikh S**, **Wyman J**, **Pantelic M**, **Song T**, **Nadig J**, **Karabon P**, **Greenbaum A**, and **O'Neill W**. Application of 3-dimensional computed tomographic image guidance to WATCHMAN implantation and impact on early operator learning curve: Single-center experience *JACC Cardiovasc Interv* 2016; 9(22):2329-2340. PMID: 27884358. Full Text

Center for Structural Heart Disease, Division of Cardiology, Henry Ford Health System, Detroit, Michigan. Electronic address: dwang2@hfhs.org.
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Division of Radiology, Henry Ford Health System, Detroit, Michigan.

OBJECTIVES: The aim of this study was to examine the impact of 3-dimensional (3D) computed tomographic (CT) guided procedural planning for left atrial appendage (LAA) occlusion on the early operator WATCHMAN learning curve. BACKGROUND: Traditional WATCHMAN implantation is dependent on 2-dimensional transesophageal echocardiographic (TEE) sizing and intraprocedural guidance. METHODS: LAA occlusion with the WATCHMAN device was performed in 53 patients. Pre-procedural case plans were generated from CT studies with recommended device size, catheter selection, and C-arm angle for deployment. RESULTS: All 53 patients underwent successful LAA occlusion with the WATCHMAN. Three-dimensional CT LAA maximal-width sizing was 2.7 +/- 2.2 mm and 2.3 +/- 3.0 mm larger than 2-dimensional and 3D TEE measurements, respectively (p </= 0.0001). By CT imaging, device selection was 100% accurate. There were 4 peri-WATCHMAN leaks (<4.5 mm) secondary to accessory LAA pedunculations. By 2-dimensional TEE maximal-width measurements alone, 62.3% (33 of 53) would have required larger devices. Using 3D TEE maximal-width measurements, 52.8% of cases (28 of 53) would have required larger devices. Three-dimensional TEE length would have inappropriately excluded 10 patients from WATCHMAN implantation. Compared with the average of 1.8 devices used per implantation attempt in PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) (82% success rate), the present site averaged 1.245 devices per implantation attempt (100% success rate). There were no intraprocedural screen failures and no major adverse cardiac events. CONCLUSIONS: Three-dimensional CT image

case planning provides a comprehensive and customized patient-specific LAA assessment that appears to be accurate and may possibly facilitate reducing the early WATCHMAN implantation learning curve.

Cardiology
Yadav PK, and **Eng MH**. A toast to no sternotomy *Catheter Cardiovasc Interv* 2016; 88(6):960-961. PMID: 27886454. Full Text

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Center for Health Policy and Health Services Research
Ahmedani BK, **Belville-Robertson T**, Hirsch A, and **Jurayj A**. An online mental health and wellness intervention supplementing standard care of depression and anxiety *Arch Psychiatr Nurs* 2016; 30(6):666-670. PMID: 27888957. Full Text

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Henry Ford Health System, Behavioral Health Services, Detroit, MI.
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Center for Health Policy and Health Services Research
Henein F, **Prabhakar D**, **Peterson EL**, **Williams LK**, and **Ahmedani BK**. A prospective study of antidepressant adherence and suicidal ideation among adults *Prim Care Companion CNS Disord* 2016; 18(6)PMID: 27907275. Article Request Form

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Center for Health Policy and Health Services Research
Hu J, and **Nerenz D**. Relationship between stress rankings and the overall hospital star ratings: An analysis of 150 cities in the united states *JAMA Intern Med* 2016;PMID: 27893893. Full Text

Center for Health Policy & Health Services Research, Henry Ford Health System, Detroit, Michigan.

Center for Health Policy and Health Services Research
Li J, **Gordon SC**, **Rupp LB**, **Zhang T**, **Trudeau S**, Holmberg SD, Moorman AC, Spradling PR, Teshale EH, Boscarino JA, Daida YG, Schmidt MA, and **Lu M**. Long-term progression of viral load and serum markers of fibrosis among treated and untreated patients with chronic hepatitis B *J Gastroenterol Hepatol* 2016;PMID: 27888529. Full Text

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BACKGROUND AND AIMS: Antiviral therapy for patients with hepatitis B (HBV) infection is generally deferred for "immune inactive" patients, although longitudinal changes in viral load and liver fibrosis remain understudied in this population. Likewise, in treated patients, the temporal relationship between changes in viral load and liver fibrosis is not well-characterized. Using data from the Chronic Hepatitis Cohort Study, we investigated viral load and the Fibrosis-4 index (FIB4, a serum-based marker of liver fibrosis) trajectories in both untreated and treated HBV patients. MATERIALS AND METHODS: We applied a bivariate, piecewise, linear spline, mixed-effects modeling approach to data from 766 HBV patients (342 untreated, 424 treated). Treatment selection bias was adjusted using propensity scores. Multiple sensitivity analyses were used to confirm results in untreated patients. RESULTS: Among all untreated patients, FIB4 began to increase by 0.9% per month (11% per year) ($p < 0.05$) at 28 months post-index date, suggesting fibrosis progression. Significant FIB4 progression was also observed within a subgroup analysis of "immune inactive" untreated patients. In treated patients, viral load declined 31.8% per month ($p < 0.05$) for the first 5 months after treatment initiation, and 1.4-1.7% per month ($p < 0.05$) thereafter. At 5 months after treatment initiation, FIB4 began to decline 0.5% per month ($p < 0.05$), stabilizing at 28 months. CONCLUSION: Among untreated HBV patients, FIB4 gradually increases over time, suggesting fibrosis progression, even in those patients designated as immune inactive. In treated patients, antiviral therapy results in a rapid decline in viral load followed by a delayed decline in markers of liver fibrosis.

Center for Health Policy and Health Services Research
Lu M, **Gordon SC**, **Li J**, **Rupp LB**, **Zhou Y**, Moorman AC, Spradling P, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, **Trudeau S**, and Holmberg SD. Hepatitis C complications: Prevalence and disparities in a large US cohort 2006-2014 *Hepatology* 2016; 63(1):95A-96A. PMID: Not assigned. Abstract

M. Lu, Public Health Science, Henry Ford Health System, Detroit, United States

The burden of hepatitis C virus (HCV)-related cirrhosis, decompensated cirrhosis, and mortality has not been well-described in a large “real world” US population. We investigated trends in the prevalence of cirrhosis and decompensated cirrhosis, and incidence of mortality, among HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS) from 2006-2014. Methods: CHeCS is a longitudinal observational study of hepatitis patients from 4 large US health systems. Cirrhosis was ascertained using ICD9 codes, liver biopsy reports, and serum markers of fibrosis. Decompensated cirrhosis was ascertained using a set of ICD9 codes that have been validated as predictive of decompensated cirrhosis. We used join-point modeling (univariate and multivariate) to identify rates of change in prevalence over time as well as “break points” that indicate different phases of Annual Percentage Change (APC). Results: Of 11,286 adult HCV-infected patients, prevalence of cirrhosis increased from 10% in 2006 to 28% in 2014. Join-point analysis identified a breakpoint at 2007, with adjusted APCs of 49.1 (2006-2007; $p<0.05$) and 9.5 (2007-2014; $p<0.05$). Prevalence of decompensated cirrhosis increased from 3% in 2006 to 7% in 2014, with two breakpoints (at 2008 and 2012) and three segments, with APCs of 25.9 (2006-2008; $p<0.05$), 8.7 (2008-2012; $p<0.05$), and 1.4 (2012-2014). Incidence of all-cause mortality increased from 1.1% in 2006 to 3.1% in 2013, with a breakpoint in 2010 and APCs of 20.0 (2006-2010; $p<0.05$) and 4.2 (2010-2013). Older patients, Asian/Pacific Islanders, and men all demonstrated higher prevalence of cirrhosis and decompensated cirrhosis. Black patients demonstrated the highest incidence of all-cause mortality. Conclusions: Over the past decade, prevalence of cirrhosis among HCV patients in this US cohort increased almost 3-fold. During the same time period, prevalence of decompensated cirrhosis and incidence of all-cause mortality more than doubled, although the increase in both plateaued in recent years (Figure Presented).

Center for Health Policy and Health Services Research
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, and Holmberg SD. Uptake of and factors associated with direct-acting antiviral therapy among patients infected with hepatitis C virus in the chronic hepatitis cohort study, 2014-2015 *Hepatology* 2016; 63(1):10A-11A. PMID: Not assigned. Abstract

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Background: Limited information is available describing the uptake of direct acting antiviral (DAA) therapy for hepatitis C virus (HCV) infection among patients in general US healthcare settings. Methods: We analyzed data collected from HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS), an observational cohort study involving patients from healthcare organizations in Michigan, Pennsylvania, Oregon, and Hawaii, limiting analysis to patients

with a clinical encounter during the previous two years. Uptake was defined as the proportion of patients infected with HCV as of December 31, 2013 who were prescribed a DAA regimen (with or without interferon) during 2014 and started the regimen by August 31, 2015. Using multivariable analysis and controlling for relevant variables, we examined demographic and clinical characteristics associated with receipt of DAAs. Results: The cohort was comprised of 10,293 HCV-infected patients as of December 31, 2013, of whom 544 (5.3%) started a DAA regimen by August 31, 2015. Factors independently associated with receipt of DAAs included higher annual income (adjusted Odds Ratios [aOR] 2.4 and 1.7 for income >$50K and $30K-$50K, respectively, vs. <$30K), higher FIB4 score (aORs 2.1, 2.0, and 1.5 for FIB4 >5.88, 3.25-5.88, 2.0-<3.25, respectively, vs. <2.0), genotype 2 infection (aOR 2.2, vs. genotype 1), higher Charlson comorbidity score (aORs 1.3 and 1.4 for scores ≥2 and 1, respectively, vs. score of 0), pre-2014 treatment failure (aOR 1.9, vs. treatment-naive), and HIV coin fection (aOR 1.9, vs. HCV monoinfection). Factors associated with a reduced likelihood of DAA receipt included non-Hispanic Black race/ethnicity (aOR 0.7, vs. non-Hispanic Whites), having Medicaid coverage (aOR 0.5, vs. private insurance), and receipt of care at one of the study sites (aOR 0.3, vs. a tertiary hepatology referral site). Sex, age, and duration of follow- up were not associated with receipt of DAAs. Conclusions: Among patients in these general US healthcare settings, uptake of DAA therapy was low from January 2014-August 2015, and especially so among minority and Medicaid patients. Targeted efforts to improve access to DAAs for these patients are essential to reduce morbidity and mortality from HCV infection.

Center for Health Policy and Health Services Research

Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, and Holmberg SD. Preliminary clinical outcome data among patients with hepatitis C virus infection receiving direct-acting antiviral therapy in the Chronic Hepatitis Cohort Study, 2014-2015 *Hepatology* 2016; 63(1):487A-488A. PMID: Not assigned. Abstract

P.R. Spradling, Division of Viral Hepatitis, CDC, Atlanta, United States

Background: Data describing clinical outcomes of direct-acting antiviral (DAA) therapy among patients infected with hepatitis C virus (HCV) in general healthcare settings are limited. We examined DAA-associated outcomes among HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS), an observational study conducted at 4 US healthcare organizations. Methods: Patients who began a DAA regimen from January 2014-August 2015 were included in the analysis. We examined frequency of treatment completion and of sustained viral response (SVR) 12 weeks post-treatment vs. no SVR by sociodemographic, clinical, and treatment-related factors, and conducted multivariable analysis to identify factors independently associated with SVR. Results: Of 613 patients who began an initial DAA regimen during the study period, 212 (48%) were treatment experienced, 210 (54%) had cirrhosis, 81 (18%) were of black race, and 24 (5%) were HIV-coinfected: 280 (46%) had HCV genotype 1a (G1a); 136 (22%) had G1b; 107 (17%) had G2; 68 (11%) had G3; 5 (1%) had G4-6; and 17 (3%) had mixed genotype infection. Overall, 401 (65%) patients received a sofosbuvir (SOF) regimen without ledipasvir (LDV) (i.e., SOF ± simeprevir or daclatasvir ± ribavirin [RBV]) and 211 (34%) received SOF with LDV ± RBV. No patients received an ombitasvir-containing regimen. Of 545 (89% of 613) patients with available SVR data, 463 (85%) achieved SVR. Among patients with G1a, frequencies of SVR ranged from 77% (SOF without LDV and no RBV) to 96% (SOF with LDV ± RBV); among those with G1b, 70% (SOF regimen without LDV + RBV) to 98% (SOF with LDV ± RBV). The frequency of SVR was 83%, 80% and 75% among patients with G2, G3, and G4-6 infection, respectively. In multivariable analysis controlling for all variables, the sole factor independently associated with SVR was receipt of SOF with LDV ± RBV (aOR 6.1 vs. SOF regimen without LDV and no RBV). Neither age, sex, race/ethnicity, previous treatment status, presence of cirrhosis, genotype, comorbidity score, body mass index, or HIV coinfection were associated with SVR. Of the 613 patients who initiated treatment, 68 (11%) either had completed treatment but did not yet have SVR data available (n=32), were still receiving treatment at the close of the study period (n=22), or stopped treatment early (n=14). Conclusions: Among patients who received DAAs in these general healthcare settings, half of whom had cirrhosis and previous treatment, the frequency of treatment completion and SVR was high. Receipt of a regimen other than SOF with LDV was associated with a lower likelihood of achieving SVR.

Center for Health Policy and Health Services Research

Teshale EH, Zhong Y, Moorman AC, Spradling PR, Holmberg SD, **Rupp LB**, **Lu M**, **Gordon SC**, Boscarino JA, Daida Y, and Schmidt MA. Alcohol use disorder among chronic hepatitis C patients: Prevalence and treatment outcome, CHeCS, 2006-2013 *Hepatology* 2016; 63(1):873A-874A. PMID: Not assigned. Abstract

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Background: Alcohol use in patients with chronic hepatitis C (CHC) results in progression of liver disease and represents a barrier to antiviral therapy. We sought to determine the prevalence of alcohol abuse and alcohol-related liver disease among CHC patients to assess their access to HCV treatment. Methods: We used CHeCS data

collected from CHC patients seen in four large U.S. healthcare systems from 2006-2013. Among patients with documented ICD 9 codes indicative of any alcohol use disorder defined as alcohol abuse/dependence and alcohol-related liver disease, we determined the percentage of patients with any alcohol disorder, with alcohol abuse/dependence, and with alcohol-related liver disease who received HCV treatment. We used multivariable analysis to identify factors associated with HCV treatment by alcohol status. Results: Of the 11,636 CHC patients, 3,553 (30.5%) had at least one documented ICD-9 code indicative of any alcohol use disorder. Among those with any alcohol use disorder, 70.4% were male, 92.5% were aged >44 years, 58.7% were white, and 19.9% had alcohol-related liver disease. Overall, 40.3% of CHC patients received HCV treatment. Only 30.4% of those with alcohol abuse and 50.4% of those with alcohol-related liver disease received treatment. Sustained virologic response rates were 41.6% overall, 44.7% for those with alcohol abuse, and 28.4% for those with alcohol-related liver disease. In univariate analysis HCV treatment was associated with age, race, household income, ever having biopsy and biopsy stage ($p<0.01$). Controlling for age, gender, race, and household income, persons with alcohol abuse were less likely [adjusted odds ratio (aOR) = 0.54 (0.48-0.61)] and those with alcohol- related liver disease were more likely [aOR =1.38 (1.18- 1.63)] to receive HCV treatment than those with no alcohol use disorder. Conclusion: Approximately one third of CHC patients had a recorded diagnosis, indicative of an alcohol use disorder. Although patients diagnosed with alcohol-related liver disease were more likely to receive HCV treatment than those with an alcohol abuse diagnosis, treatment and the response to treatment for patients with either diagnosis were suboptimal overall. Effective direct acting antiviral treatment with greater tolerability and of shorter duration may improve the likelihood of treatment and treatment outcome among all patients, including those with an alcohol use disorder.

Dermatology

Almario L, **Antonyan AS**, **Porto DA**, Gomez-Roberts H, Alhousseini A, and Gonik B. Management of psoriasis herpeticum in pregnancy: A clinical conundrum *Case Rep Obstet Gynecol* 2016; 2016:5319425. PMID: 27840756. Full Text

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Introduction. Kaposi varicelliform eruption (KVE) is a widespread cutaneous viral infection, most commonly herpes simplex virus, which affects patients with underlying dermatosis. When KVE occurs in a patient with a history of psoriasis, it is referred to as psoriasis herpeticum, a rare subtype of KVE with only a handful of cases reported in the literature. To the authors' knowledge, we report for the first time a case of psoriasis herpeticum in pregnancy. Case Presentation. A 23-year-old woman in her third pregnancy presented at 26-week gestation with a 10-year history of psoriasis. Cutaneous examination revealed diffuse psoriatic plaques with scattered ~1 cm erosions. Punch biopsy of the skin revealed herpes simplex virus (HSV) infection within a psoriatic plaque, necessitating dermatological treatment. The patient experienced premature rupture of membranes at 37-week gestation. Pelvic exam showed no evidence of herpetic lesions. After labor augmentation, the patient delivered a healthy female infant with no evidence of HSV infection. Discussion. Psoriasis herpeticum is a rare and potentially devastating complication of an underlying dermatosis. With a paucity of data available to guide pregnancy-specific issues, the general management of this condition is controversial and requires a multidisciplinary care approach. Concerns for systemic infection in the mother and vertical transmission to the neonate are of critical importance.

Dermatology

Gan EY, Eleftheriadou V, Esmat S, **Hamzavi I**, Passeron T, Bohm M, Anbar T, Goh BK, Lan CE, Lui H, Ramam M, Raboobee N, Katayama I, Suzuki T, Parsad D, Seth V, **Lim HW**, van Geel N, Mulekar S, Harris J, Wittal R, Benzekri L, Gauthier Y, Kumarasinghe P, Thng ST, Silva de Castro CC, Abdallah M, Vrijman C, Bekkenk M, Seneschal J, Pandya AG, Ezzedine K, Picardo M, and Taieb A. Repigmentation in vitiligo: Position paper of the vitiligo global issues consensus conference (VGICC) *Pigment Cell Melanoma Res* 2016;PMID: 27864868. Full Text

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The Vitiligo Global Issues Consensus Conference (VGICC), through an international e-Delphi consensus, concluded that "repigmentation" and "maintenance of gained repigmentation" are essential core outcome measures in future vitiligo trials. This VGICC position paper addresses these core topics in two sections and includes an atlas depicting vitiligo repigmentation patterns and color match. The first section delineates mechanisms and characteristics of vitiligo repigmentation and the second summarizes the outcomes of international meeting discussions and two e-surveys on vitiligo repigmentation, which had been carried out over three years. Treatment is defined as successful if repigmentation exceeds 80% and at least 80% of the gained repigmentation is maintained for over 6 months. No agreement was found on the best outcome measure for assessing target or global repigmentation, therefore highlighting the limitations of e-surveys in addressing clinical measurements. Until there is a clear consensus, existing tools should be selected according to the specific needs of each study. A workshop will be conducted to address the remaining issues so as to achieve a consensus.

Dermatology
Hamzavi IH, **Zarbo A**, and **Lim HW**. Reply to: "Re: Comorbid autoimmune diseases in patients with vitiligo: A cross-sectional study" *J Am Acad Dermatol* 2016; 75(6):e233. PMID: 27846973. Full Text

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Dermatology
Isaacs SR, **Wang J**, Kim KW, **Yin C**, **Zhou L**, **Mi QS**, and Craig ME. MicroRNAs in type 1 diabetes: Complex interregulation of the immune system, beta cell function and viral infections *Curr Diab Rep* 2016; 16(12):133. PMID: 27844276. Full Text

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Since the discovery of the first mammalian microRNA (miRNA) more than two decades ago, a plethora of miRNAs has been identified in humans, now amounting to more than 2500. Essential for post-transcriptional regulation of gene networks integral for developmental pathways and immune response, it is not surprising that dysregulation of miRNAs is often associated with the aetiology of complex diseases including cancer, diabetes and autoimmune disorders. Despite massive expansion of small RNA studies and extensive investigation in diverse disease contexts, the role of miRNAs in type 1 diabetes has only recently been explored. Key studies using human islets have recently implicated virus-induced miRNA dysregulation as a pivotal mechanism of beta cell destruction, while the interplay between miRNAs, the immune system and beta cell survival has been illustrated in studies using animal and cellular models of disease. The role of specific miRNAs as major players in immune system homeostasis highlights their exciting potential as therapeutics and prognostic biomarkers of type 1 diabetes.

Dermatology

Naka F, **Shwayder TA**, and Santoro FA. Photodermatoses: Kids are not just little people *Clin Dermatol* 2016; 34(6):724-735. PMID: Not yet assigned. Full Text

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Photodermatoses are a group of skin disorders caused by abnormal reaction to ultraviolet radiation. Photodermatoses are divided into four groups: (1) immunologically mediated photodermatoses; (2) chemical- and drug-induced photodermatoses; (3) photoaggravated dermatoses; and (4) hereditary photodermatoses. This contribution discusses differences in the approach and diagnosis of pediatric and adult patients with suspected photodermatoses, focusing on immunologically mediated photodermatoses and chemical- and drug-induced photodermatoses.

Emergency Medicine

Beri N, Marston NA, Daniels LB, **Nowak RM**, Schreiber D, Mueller C, Jaffe A, Diercks DB, Wettersten N, DeFilippi C, Peacock WF, Limkakeng AT, Anand I, McCord J, **Hollander JE**, Wu AH, Apple FS, Nagurney JT, Berardi C, Cannon CM, Clopton P, Neath SX, Christenson RH, Hogan C, Vilke G, and Maisel A. Necessity of hospitalization and stress testing in low risk chest pain patients *Am J Emerg Med* 2016;PMID: 27847253. Full Text

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BACKGROUND: Copeptin is a marker of endogenous stress including early myocardial infarction(MI) and has value in early rule out of MI when used with cardiac troponin I(cTnI). OBJECTIVES: The goal of this study was to demonstrate that patients with a normal electrocardiogram and cTnI<0.040mug/l and copeptin<14pmol/l at presentation and after 2 h may be candidates for early discharge with outpatient follow-up potentially including stress testing. METHODS: This study uses data from the CHOPIN trial which enrolled 2071 patients with acute chest pain. Of those, 475 patients with normal electrocardiogram and normal cTnI(<0.040mug/l) and copeptin<14pmol/l at presentation and after 2 h were considered "low risk" and selected for further analysis. RESULTS: None of the 475 "low risk" patients were diagnosed with MI during the 180day follow-up period (including presentation). The negative predictive value of this strategy was 100% (95% confidence interval(CI):99.2%-100.0%). Furthermore no one died during follow up. 287 (60.4%) patients in the low risk group were hospitalized. In the "low risk" group, the only difference in outcomes (MI, death, revascularization, cardiac rehospitalization) was those hospitalized underwent revascularization more often (6.3%[95%CI:3.8%-9.7%] versus 0.5%[95%CI:0.0%-2.9%], p=.002). The hospitalized patients were tested significantly more via stress testing or angiogram (68.6%[95%CI:62.9%-74.0%] vs 22.9%[95%CI:17.1%-29.6%], p<.001). Those tested had less cardiac rehospitalizations during follow-up (1.7% vs 5.1%, p=.040). CONCLUSIONS: In conclusion, patients with a normal electrocardiogram, troponin and copeptin at presentation and after 2 h are at low risk for MI and death over 180days. These low risk patients may be candidates for early outpatient testing and cardiology follow-up thereby reducing hospitalization.

Emergency Medicine

Macedo M, **Kim B**, **Khoury R**, and **Narkiewicz L**. A rare case of right lower quadrant abdominal pain *Am J Emerg Med* 2016;PMID: 27842925. Full Text

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Isolated fallopian tube torsion without involvement of the ovary is a rare condition most frequently presenting during reproductive years. Imaging, vitals, physical exam, and laboratory findings all fail to help establish a definitive diagnosis. The majority of the diagnoses are made on the operating table. Physical exam most often reveals unilateral and localized abdominal pain, often with nausea and vomiting, but few other reliably common findings. Diagnosis becomes even more challenging due to the fact that isolated tubal torsion occurs often in pregnancy and preferentially on the right, further complicating the clinical picture. We describe a case of isolated tubal torsion, unique in that localized necrosis and inflammation from the torsion triggered a secondary appendicitis. The patient required surgical intervention, and an appendectomy and salpingectomy emergently. Given its elusive and rare nature, awareness and early intervention is required by the emergency physician to recognize tubal torsion, as operative intervention is crucial, and can lead to preservation of fertility and improved fetal survival.

Endocrinology and Metabolism

He F, Zhang W, Shen Y, Yu P, Bao Q, Wen J, Hu C, and **Qiu S**. Effects of resection margins on local recurrence of osteosarcoma in extremity and pelvis: Systematic review and meta-analysis *Int J Surg* 2016; 36(Pt A):283-292. PMID: 27840310. Full Text

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PURPOSE: There are conflicting findings about the effect of resection margins on local recurrence in osteosarcoma after surgery. In this meta-analysis, we examined the association between local recurrence and resection margins for osteosarcoma in extremity and pelvis. METHODS: EMBASE, PubMed and Cochrane CENTRAL were searched from January 1980 to July 2016. The quality of included studies was evaluated using the Newcastle-Ottawa Quality Assessment Scale. The odds ratio and 95% confidence interval of local recurrence were estimated, respectively, for inadequate vs adequate margins and marginal vs wide margins using a random-effect model. Chi-square test was performed to comparing the local recurrence rate between extremity and pelvic osteosarcomas with an identical surgical margin. RESULTS: Thirteen articles involving 1559 patients (175 with and 1384 without local recurrence) were included in this study. The meta-analysis showed that the osteosarcoma resected with inadequate and marginal margins, whether in extremity or in pelvis, were associated with a significantly higher local recurrence rate than the osteosarcoma resected with adequate and wide margins, respectively. Chi-square test showed that, when pelvic and extremity osteosarcomas were removed with an identical resection margin, the local recurrence was significantly more frequent in pelvis osteosarcoma than in extremity osteosarcoma. CONCLUSION: This study provides level IIa evidence to support that the surgery with adequate or wide resection margin has positive effect on reducing the risk of local recurrence in osteosarcoma. In addition, the factors independent of resection margin are more likely to increase the risk of local recurrence in pelvic osteosarcoma. LEVEL OF EVIDENCE: Level IIa, Therapeutic study.

Endocrinology and Metabolism

Putnam R, Dhibar DP, Varshney S, Behera A, Mittal BR, Bhansali A, **Rao SD**, and Bhadada SK. Effect of curative parathyroidectomy on insulin resistance *Indian J Endocrinol Metab* 2016; 20(6):784-789. PMID: 27867880. Full Text

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BACKGROUND: Primary hyperparathyroidism (PHPT) is characterized by inappropriately elevated serum parathyroid hormone (PTH) level despite elevated serum calcium. Insulin resistant is the basic pathophysiology, behind the higher prevalence of diabetes mellitus in patients with PHPT. However, the improvement in insulin resistance (IR) after curative parathyroidectomy (CPTX) has not been established yet, as the study results are conflicting. MATERIALS AND METHODS: In this prospective interventional study, ten patients with mild PHPT (Group 1) and another ten patients with moderate to severe PHPT (Group 2) were undergone CPTX. The IR was assessed by homeostasis model assessment-IR (HOMA-IR), quantitative insulin sensitivity check index (QUICKI), fasting plasma glucose (FPG), and fasting serum insulin (FSI), before and 3 months after CPTX. RESULTS: There was no significant change of FPG and FSI, before and after CPTX in Group 1 (P = 0.179 and P = 0.104) and Group 2 (P = 0.376 and P = 0.488). Before surgery, HOMA-IR was higher, and QUICKI was significantly lower, in both Group 1 (P = 0.058 and P = 0.009) and Group 2 (P = 0.023 and P = 0.005) as compared to published normal reference mean, with no significant difference between the groups. Three months after surgery HOMA-IR increased further and QUICKI remained unchanged as compared to baseline, in both Group 1 (P = 0.072 and 0.082) and Group 2 (P = 0.54 and 0.56), but statistically insignificant. CONCLUSION: IR remained unchanged after CPTX in mild as well as moderate to severe PHPT. Asymptomatic PHPT with abnormal IR should not be used as criteria for parathyroidectomy.

Gastroenterology

Agrawal S, **Hussain S**, **Elbatta M**, **Markus J**, **Jafri SM**, and **Ibrahim M**. Adenomyomatous polyp of the duodenum: A phenomenon seen rarely *Am J Gastroenterol* 2016; 111:S987. PMID: Not assigned. Abstract

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Introduction:. Adenomyoma of the gastrointestinal tract is an infrequent benign nonneoplastic tumorlike lesion. Endoscopic and radiologic evaluations are by no means pathognomic, and tissue diagnosis is essential for its accurate diagnosis. We describe the case of an incidentally found adenomyoma of the duodenum. Case: A 68-year-

old African American male, with Bilroth II anatomy for gastric cancer, presented with symptoms of reflux and dysphagia to solid food. His previous surveillance endoscopy appeared normal. He denied other alarm symptoms. Physical examination was unremarkable. On EGD, there was visualization of surgical anatomy as well a 15 mm polyp in the blind loop corresponding to the duodenum. There were no findings to explain his symptoms. Biopsies were obtained of the esophagus, stomach and duodenal polyp. On histology, there was H.pylori gastritis of the stomach without dysplasia. The polyp histology showed nodular proliferation of benign branching glands lined by bland cuboidal to columnar cell lining within a smooth muscle stroma. This was consistent with an adenomyomatous polyp without any evidence of atypia or malignancy. Discussion: Adenomyomatous polyps of the duodenum are extremely rare. Only one case of a duodenal adenomyoma is reported in the last ten years. Of the 26 cases of adenomyomas of the small intestine, all were found in the jejunum and ileum. Histologically, they have abnormal glands without atypia in a mesenchymal stroma, lined by cuboidal or columnar cells. There are various theories of the etiology of adenomyomas, indicating they may be a form of epithelial hamartoma or alternatively a form of heterotopic pancreatic tissue. The majority of these benign tumors occur in the pyloric region of the stomach and are generally asymptomatic although they may cause abdominal pain, biliary obstruction, intussusception, and intestinal obstruction. Adenomyomatous tumors can be difficult to diagnose preoperatively, as histologic confirmation is often needed. Symptoms and radiologic imaging may suggest malignant disease, resulting in unnecessary surgical intervention. Given the rarity of this entity, no management guidelines for asymptomatic adenomyomas exist. Conclusion: Duodenal adenomyomas are a rare gastrointestinal finding. We wanted to take this opportunity to increase clinician awarenessof this entity and also to generate discussion regarding optimal approach of management, for which no guidelines currently exist.

Gastroenterology

Agrawal S, **Mullins K**, **Tosch K**, **Muszkat Y**, and **Jafri SM**. Single-center experience in concurrent use of ombitasvir/paritaprevir/ritonavir with dasabuvir and tacrolimus for recurrent hepatitis C after liver transplantation *Am J Gastroenterol* 2016; 111:S907-S908. PMID: Not assigned. Abstract

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Purpose: We present a single center experience of ombitasvir/paritaprevir/ritonavir with dasabuvir (OPRD) to treat chronic hepatitis C (HCV) infection in patients who underwent orthotopic liver transplantation, demonstrating its potential to increase tacrolimus levels leading to nephrotoxicity, and methods to avoid injury. Methods: Retrospective chart review of patients post-liver transplant HCV genotype 1 disease treated with OPRD. Data included demographics, HCV genotype, HCV RNA level, tacrolimus levels on therapy, and renal function at baseline and during treatment. Results: The first patient treated with OPRD was a 61 year old male with recurrent HCV, genotype 1b, status-post liver transplant 4 years prior. Patient initiated a 12 week course of OPRD therapy without notifying transplant staff while concurrently taking 1.5 mg of tacrolimus daily. No dose adjustments were made or labs drawn for two weeks. He was then noted to have a tacrolimus level of 60, a creatinine of 3.29mg/dL (baseline 1.4mg/dL), and potassium of 6.1mmol/L. Tacrolimus was held but renal dysfunction persisted for 1 month. OPRD was continued. Renal biopsy showed acute tubular necrosis likely due to tacrolimus-induced injury. By the end of the treatment period, creatinine trended down to 2.17mg/dL with tacrolimus level less than 3. The patient was then started on 0.5 mg of tacrolimus twice daily. Most recent laboratory values 7 months after finishing treatment show continued HCV RNA suppression and a creatinine of 2.52 mg/dL. The second patient was a 54 year old male with recurrent Hepatitis C cirrhosis, genotype 1a, in his liver transplanted 14 years prior. He was treated with OPRD with ribaviran with suppression of HCV RNA after 6 weeks of treatment. Before initiating OPRD, his tacrolimus dose was reduced from 0.5 mg twice daily to 0.5 mg weekly. Labs were drawn weekly. Throughout therapy, tacrolimus levels remained in normal limits. There is continued viral suppression without kidney dysfunction. His creatinine after finishing treatment with OPRD with ribavirin was 0.83mg/dL, which is approximately his baseline. Conclusion: OPRD used to treat HCV in liver transplant patients has risk for serious drug-drug interactions. With dose adjustments and monitoring of tacrolimus levels and creatinine, potential nephrotoxicity may be avoided.

Gastroenterology

Aguin V, **Bhatti F**, **El Atrache M**, and **Kaur N**. An unusual case of polypoid vascular ectasia *Am J Gastroenterol* 2016; 111:S732-S733. PMID: Not assigned. Abstract

V. Aguin, Henry Ford Health System, Detroit, United States

62 years old male patient underwent routine screening colonoscopy. He was found to have diffuse erythema, friability and colitis along with multiple large polyps. Biopsies suggested vascular ectasia without dysplasia. He had no symptoms and no history of gastrointestinal (GI) bleeding. He denied family or personal history of liver disease. Two months later, he underwent an EGD and another colonoscopy. Large polyps were found throughout the colon (see

figures). Adenomatous tissue was reported on biopsies. He also had new esophageal and rectal varices as well as ectatic vessels in the stomach. Liver CT showed marked intraabdominal varices in the jejunum and gastric wall. Findings were consistent with portal hypertension. Full workup including viral hepatitis, autoimmune liver disease, iron overload, HIV, giardia, cryptosporidium, schistosomiasis and parasites were all negative. Endoscopies were performed again 5 months later. There was an extensive, diffuse, pan-colonic polypoid hypervascular lesions. Findings appeared nearly identical to initial exam. There were multiple patches of vascular ectasia lesions in the duodenum. Biopsies were all negative for dysplasia. Liver biopsy was pursued and showed minimal to mild portal inflammation with mild macrovesicular steatosis. Discussion: Portal hypertension is characterized by vascular ectatic changes in stomach and colon termed portal gastropathy and colopathy, respectively. Vascular ectasias are the most common vascular lesions in the GI tract and probably the most frequent cause of recurrent or chronic lower GI bleeding in the elderly population. Endoscopically, they appear as flat or slightly elevated bright red lesions. There are only few cases of polypoid vascular ectasias reported. These were manly solitary and usually located in the transverse, descending and sigmoid colon. Portal hypertensive colopathy (PHC) is prevalent in 25-70% of patient with cirrhosis. The incidence of vascular ectasia detected by colonoscopy has been reported to range from 1% to 6%. There is no established standard treatment of PHC. There might be a role for β-blockers for primary or secondary prophylaxis for lower GI bleeding caused by PHC. In summary, polypoid vascular ectasias and portal hypertensive gastropathy are important clinically because they may lead to chronic and/or acute GI bleeding. Careful investigation is essential to accurately delineate the proper diagnostic needs and to start specific treatment. (Figure Presented).

Gastroenterology
Aguin V, **Meighani A**, **Hussain S**, **Atrache ME**, **Elbatta M**, **Bukannan A**, **Jafri SM**, and **Ibrahim M**. Elevated head of the bed, a novel position for performing colonoscopy: Does it improve the quality of the examination? *Am J Gastroenterol* 2016; 111:S141. PMID: Not assigned. Abstract

V. Aguin, Henry Ford Health System, Detroit, United States

Introduction: Colonoscopy is currently considered to be the gold standard for colon cancer screening. Cecal intubation rate, withdrawal time and adenoma detection rate are acknowledged as quality measures for colonoscopy. We feel that terminal ileum intubation rate would add to the diagnostic quality of colonoscopy. Shortening of cecal intubation time and total procedure time would improve the patient comfort and the economics of the procedure. We evaluated the impact of elevating the head of the bed on these quality measures of colonoscopy. Methods: We performed a retrospective electronic medical records (EMR) review of 655 patients who had their screening colonoscopy at a teaching tertiary care hospital. Descriptive analyses and group comparisons were performed between two groups. One group (N = 323) had their colonoscopy performed in a flat left lateral position and the second group (N= 332) had their colonoscopy with the head of the bed elevated 30 degrees. We collected data on their baseline characteristics, cecal intubation time, withdrawal time, total procedure time, terminal ilium intubation, and polyp detection rate. Differences between groups for time variables were tested via independent samples t-tests, while associations between categorical variables and head position were tested with chi-square tests. Results: Elevated position increased the terminal ilium intubation rate to 78.71 % compared to 69.95 % in the standard flat position (p-0.007). Cecal intubation time (mean of 6.35 min), withdrawal time (mean of 10.63 min) and total procedure time (mean of 16.85 min) in the tilted position, were shorter than in the flat position mean of (6.49 min, 10.80 min, and 17.20 min, respectively) (p-0.644, 0.687, 0.499). The polyp detection rate was (53.27%) for the elevated position, which is minimally higher than that for flat position (53.16%). Conclusion: Patients with tilted head of the bed had statistically significant higher rate of terminal ilium intubation, compared to those with a standard flat position. There was a shortening of cecal Intubation time and total procedure time in the tilted position, but it was not statistically significant. In the elevated head group the quality of the examination was not compromised by the faster procedure as indicated by the slightly higher polyp detection rate. A larger number of procedures need to be evaluated in the future to futher assess the positive effects of elevation of the head of the bed on all the quality measures of colonoscopy.

Gastroenterology
Ahmed A, Saab S, **Gordon SC**, Dieterich DT, Wong RJ, **Brown KA**, Kugelmas M, and Younossi ZM. A decision analytic markov model to evaluate the health outcomes of sofosbuvir/velpatasvir for patients with chronic hepatitis C virus genotypes 1 to 6 and decompensated cirrhosis in the US *Hepatology* 2016; 63(1):418A. PMID: Not assigned. Abstract

A. Ahmed, Stanford University Medical Center, Stanford, United States

BACKGROUND AND AIM: Chronic hepatitis C virus (CHC) patients with decompensated cirrhosis (DCC) awaiting transplant have limited treatment options and are at high risk for liver-related comorbidity and increased mortality.

The new oral single tablet regimen of sofosbuvir/velpatasvir (SOF/VEL) has been shown to have excellent efficacy and safety in this population. A decision-analytic Markov model evaluated the health outcomes of SOF/VEL compared with current treatment options in DCC. METHODS: The analysis modeled a cohort of 10,000 CHC DCC genotype (GT) 1-6 patients with an average age of 52 from a US third-party payer perspective over a lifetime horizon. Pre-transplant treatment with SOF/VEL for 12 weeks (W) with ribavirin (R) was compared with ledipasvir/sofosbuvir (LDV/SOF) 12W+R and 24W+/-R, SOF+ daclatasvir (DCV) for 12W+R or 24W, and no treatment (NT). Sustained virologic response (SVR) rates were extrapolated from ASTRAL-4, SOLAR-1, -2, and ALLY-1. Transition probabilities and utilities were based on a literature review and consensus by a panel of hepatologists. RESULTS: The SOF/VEL regimen resulted in the best health outcomes in terms of the lowest number of hepatocellular carcinoma (HCC) cases, liver transplants (LT), and liver-related deaths compared with all comparators in GT 1, 2, 3, and 5/6 (Table 1). In GT4, SOF+DCV was associated with slightly fewer liver-related complications, particularly for HCC and LT. CONCLUSIONS: Compared to currently available options including SOF+DCV, LDV/SOF and NT, SOF/VEL demonstrated better overall health outcomes in DCC patients, leading to fewer cases of liver-related complications. Further, SOF/VEL is the only available pan-genotypic, all-oral, oncedaily single tablet regimen for CHC patients, simplifying treatment across GTs. (Table Presented).

Gastroenterology
Alali F. A rare case of pneumatosis intestinalis *Am J Gastroenterol* 2016; 111:S1366. PMID: Not assigned. Abstract

F. Alali, Henry Ford Health System, Franklin, United States

Pneumatosis intestinalis is an uncommon disorder characterized by the presence of gas within the wall of small or large intestine. We report a case in which a patient with rheumatoid arthritis on long term steroid therapy developed pneumatosis intestinalis. An 85 year old female with history of rheumatoid arthritis on prednisone for eight years presented to the hospital with complaints of nausea, vomiting and abdominal pain which were intermittent for the last two years, but got worse two weeks before admission. On admission, her lactic acid level was mildly elevated. CT scan of her abdomen showed multiple dilated loops of small bowel with wall thickening suggestive of pneumatosis. The findings raised concern for ischemic event, especially because of evidence of gas in the portal vein. General surgery team suggested exploratory laparotomy, but the patient declined the surgery and opted for conservative management. Next day, patient's lactic acid levels normalized and she tolerated oral diet. Her diet was advanced slowly and she was discharged on tapered dose of prednisone. Given the chronicity and recent worsening of her symptoms, we concluded that ischemia was unlikely the reason for patient's symptoms. On further review of literature, patient's history and medications, it was concluded that long term steroid use could lead to Pneumatosis intestinalis. For long term management of rheumatoid arthritis, steroids are never a safe option and patients should be treated with steroid sparing drugs. In this case, steroid usage caused a rare and life threatening complication, which was pneumatosis intestinalis.

Gastroenterology
Arnautovic J, **Brown P**, and Tereziu S. Omesartan induced sprue-like enteropathy *Am J Gastroenterol* 2016; 111:S1364. PMID: Not assigned. Abstract

J. Arnautovic, Henry Ford Macomb Hospital, Clinton Township, United States

Olmesartan is a commonly prescribed antihypertensive that blocks the angiotensin receptor. A serious side effect of sprue-like enteropathy has been documented. Severe chronic diarrhea with substantial weight loss can occur months and up to years after initiation of the drug. Histologically, it is indistinguishable from celiac disease, with villous blunting; however, celiac serology is negative. The infrequency in which it is encountered makes diagnosis difficult; nevertheless, this is a newly recognized and documented side effect seen across the country. A 67-year-old male presented to the hospital with chronic diarrhea. Bowel movements were described as loose, watery, non-bloody voluminous stools without abdominal pain. Stool output was 10-12 liters daily. On admission, workup included infectious, inflammatory, absorptive and autoimmune causes. Secretory causes were ruled out as levels of calcitonin, gastrin, vasoactive intestinal peptide and 5-hydroxyindoleacetic acid were nonremarkable with a negative octreoscan. Infectious causes were ruled out with negative stool studies and viral serologies. The patient's stay was complicated by acute kidney injury, severe protein malnutrition, and pneumatosis intestinalis. Esophagogastroduodenoscopy with duodenal biopsies showed marked villous blunting consistent with celiac disease; however, serology was negative. After extensive workup, it was concluded that the patient's olmesartan was a likely etiology, as studies have shown that the medication can cause sprue-like enteropathy. Olmesartan was discontinued at admission secondary to acute kidney injury, and diarrhea resolved after 4 weeks of hospitalization. This case illustrates the possibility for severe enteropathy with the use of olmesartan and the importance of a medication review in similar cases. Olmesartan induced sprue-like enteropathy can develop months to years after the initiation of therapy and can lead to prolonged

hospital stays. One mechanism hypothesized is a cell-mediated immune response. Although very rare, enteropathy is a known adverse effect and prompt recognition is critical to resolve enteropathy, decrease unnecessary tests, and minimize hospital stay length.

Gastroenterology
Arnautovic J, **Mazhar A**, and Tereziu S. Isolated congenital asplenia: A rare case of small bowel arteriovenous malformation associated bleeding and literature review *Am J Gastroenterol* 2016; 111:S1365. PMID: Not assigned. Abstract

J. Arnautovic, Henry Ford Macomb Hospital, Clinton Township, United States

Isolated congenital asplenia is a poorly understood and a rare form of primary immunodeficiency. It can be fatal in early childhood or complicated with life-threatening infections. We encountered a unique adult case of isolated congenital asplenia associated with iron deficiency anemia and occult gastrointestinal bleeding. A 22-year-old adopted Caucasian male with a past medical history of congenital asplenia presented with weakness and recurrent melena. The patient was diagnosed with congenital asplenia at 2 years of age and microcytic anemia at 15 years of age. Extensive anemia workup did not lead to a plausible explanation. On physical examination, the patient did not have cutaneous or mucosal telangiectasis. Echocardiogram revealed no detectable situs abnormalities or cardiac defects. Endoscopy revealed multiple bleeding from duodenal and jejunal arteriovenous malformations. Profuse bleeding at the biopsy site was treated with 2 hemoclips and an epinephrine injection. Six months later, the patient reported no further episodes of gastrointestinal bleeding. This is the first reported case of isolated congenital asplenia in the United States associated with jejunal arteriovenous malformation bleeding. The differential includes Ivemark syndrome and hereditary hemorrhagic telangiectasia. Because there were no cardiovascular defects, Ivemark syndrome was ruled out. Our patient is adopted and had no other stigmata of hereditary hemorrhagic telangiectasia. Also, jejunal arteriovenous malformation are not typically seen in hereditary hemorrhagic telangiectasia. Only 16 adult cases of isolated congenital asplenia were identified and analyzed since the first reported case. Associated findings in cases of asplenia include thrombocytosis, mesenteric vein thrombosis, and pneumococcal sepsis. However, none of the cases of asplenia reported arteriovenous malformation bleeding in the adult population. One similar pediatric case has been reported in Europe. The theory of a new congenital syndrome can be proposed. However, due to the rarity of this condition, more prospective studies are needed to confirm our theory.

Gastroenterology
Bourlière M, **Gordon SC**, Ramji A, Ravendhran N, Tran TT, Hyland RH, Zhang J, Dvory-Sobol H, Stamm LM, Brainard DM, Subramanian M, McHutchison JG, Younes Z, Curry MP, Schiff ER, Reddy KR, and Manns MP. Sofosbuvir/velpatasvir/voxilaprevir for 12 weeks as a salvage regimen in NS5A inhibitor-experienced patients with genotype 1-6 infection: The phase 3 POLARIS-1 study *Hepatology* 2016; 63(1):102A-103A. PMID: Not assigned. Abstract

M. Bourlière, Hospital Saint Joseph, Marseille, France

Introduction: NS5A inhibitors are potent direct acting antiviral agents (DAAs) which are key components of HCV treatment regimens. In combination with other DAAs, NS5A inhibitors provide HCV treatments which cure over 90% of patients. For patients who have failed a regimen with an NS5A inhibitor, there is concern about long-lasting NS5A resistance-associated substitutions and currently no approved retreatment option. Sofosbuvir (SOF) and velpatasvir (VEL) are pangenotypic inhibitors of the HCV NS5B and NS5A proteins, respectively, and voxilaprevir (VOX, GS-9857) is a pangenotypic HCV NS3/4A protease inhibitor. This Phase 3 study evaluates treatment with a SOF/VEL/VOX fixed dose combination (FDC) for 12 weeks in patients who previously received an NS5A inhibitor. Methods: Patients at 108 sites in North America, Europe, Australia and New Zealand were enrolled. Eligible patients received at least 4 weeks of a prior NS5A inhibitor-containing regimen which was not discontinued due to an adverse event or unsuccessful due to non-compliance. Those with HCV genotype (GT) 1 were randomized 1:1 to receive SOF/VEL/ VOX (400mg/100mg/100mg) or matching placebo daily for 12 weeks, stratified by the presence or absence of cirrhosis. Patients of all other GTs were assigned to receive SOF/VEL/ VOX for 12 weeks. Those patients assigned to receive placebo will be offered deferred treatment with SOF/VEL/VOX for 12 weeks. The primary endpoint evaluates the superiority of the sustained virologic response 12 weeks after treatment (SVR12) to a pre-specified performance goal of 85%. Results: Of 415 patients treated, 77% were male, 78% were white, 18% had the IL28B CC genotype, 41% had compensated cirrhosis, 57% were from the US and 73% had GT 1 HCV infection. The majority of patients had DAA experience with an NS5A inhibitor given in combination with an NS5B inhibitor, and the most common prior treatment regimen was ledipasvir/SOF (66%). Treatment with SOF/VEL/VOX has been well tolerated; at the time of abstract submission, two patients have discontinued therapy due to adverse events not related to study drug, one due to chest pain, confusion, dizziness and blurred vision and another due to grade 4

elevations in transaminases, present prior to initiation of therapy. No serious adverse events attributed to study medication have been reported. Complete safety and SVR12 data for all patients will be presented. Conclusions: The single tablet regimen of SOF/VEL/VOX for 12 weeks has the potential to be a safe, well tolerated and effective treatment for patients who previously failed an NS5A inhibitor-containing DAA regimen, a group that currently has no retreatment option.

Gastroenterology
Brown P, **Parekh R**, and **Zalawadia A**. A rare case of abdominal tuberculosis *Am J Gastroenterol* 2016; 111:S1032-S1033. PMID: Not assigned. Abstract

P. Brown, Henry Ford Health System, Detroit, United States

Case: A 43-year-old Filipino female with no significant past history presented to the hospital for a two week history of abdominal pain, fever, chills, and body aches. She was found to have fever (100.8 F) and tachycardia (110/min). Ultrasound of her abdomen showed ascites and she underwent paracentesis removing 800 cc of ascitic fluid. It showed1958 white blood cells (WBC) with 71% lymphocytes and a Serum Ascitic albumin gradient (SAAG) of 0.5. She underwent computed tomographic (CT) scan of the abdomen which showed increased soft tissue density to the omentum, suggesting possibility of omental metastasis. Tumor marker CA-125 level was elevated (235). Pelvic ultrasound showed no evidence of ovarian mass. Thpatient underwent upper endoscopy (EGD) and colonoscopy which revealed five small, non-bleeding ulcers in the ascending colon. Multiple biopsies were obtained which showed non-necrotizing granulomas, negative for fungi and mycobacterium. Patient underwent interventional radiology (IR) guided biopsy of omentum which was negative for malignancy, fungi, or mycobacterium and showed non-necrotizing granulomas. The ascitic fluid culture was negative for tuberculous bacilli. Patient received a Tuberculosis skin test which was positive, 21 mm. She had immigrated from the Philippines where she was exposed. A presumptive diagnosis of peritoneal tuberculosis was made. Patient was started on TB therapy, rifampin, isoniazid, pyrazinamide & ethambutol. After six months of treatment, patient responded well to therapy with resolution of recurrent ascites and abdominal pain. Discussion: TB can involve nearly any tissue or organ and the peritoneum is one of the most common extrapulmonary sites of tuberculous infection. We describe a difficult case of peritoneal TB presenting as an abdominal malignancy. Pathology from colon ulcerations showed non-necrotizing granulomas. While an uncommon finding, reports have documented both cases of pulmonary and extrapulmonary TB with findings of non-caseating granulomas and these diagnoses were confirmed via laboratory testing. Our case was further complicated with negative lab results for TB which can be seen in upto 15% of patients. Conclusion Prompt and accurate diagnosis of peritoneal tuberculosis is essential but remains a challenge because of its nonspecific symptoms. Given the challenges of laboratory testing, TB should be considered in high risk patients with these symptoms and early intervention should be considered.

Gastroenterology
Chhatwal J, Chen Q, Ayer T, Kanwal F, Kowdley KV, Wang X, Roberts MS, and **Gordon SC**. Patients who fail treatment in the era of DAAs: Projections from HEP-SIM Model *Hepatology* 2016; 63(1):412A. PMID: Not assigned. Abstract

J. Chhatwal, Institute for Technology Assessment, Massachusetts General Hospital, Harvard Medical School, Boston, United States

Purpose: The introduction of oral direct-acting antivirals (DAAs) has dramatically changed the landscape of HCV treatment. Many more patients are eligible for therapy due to the absence of interferon and ribavirin, and real-world effectiveness mirrors the results of Phase 3 clinical trials. Our objective was to quantify the number of HCV (GT 1-6) patient population who fail on currently approved oral DAAs (including NS5A vs. non-NS5A failures) over time in the U.S. Methods: We used our Hepatitis C Disease Burden Simulation model (HEP-SIM), which was previously validated with NHANES and CDC studies and used to project changes in HCV prevalence in the U.S. We simulated the current clinical management of HCV including the birth-cohort and risk-based screening. Using market research data from IMS and IPSOS, we modeled DAA treatment in different waves starting with the launch of 1st-generation DAAs in 2011, followed by 2nd-generation DAAs including sofosbuvir, simeprevir and ledipasvir in 2014, and multiple NS5A-inhibitor containing DAAs in 2015. SVR rates were obtained from real-world TRIO and TARGET datasets. Within our model, patients who failed an NS5A were not eligible for NS5A re-treatment until 2018, unless they were cirrhotic. We projected the number of patients undergoing treatment between 2014 and 2020; and the number of patients who failed DAAs (NS5A and non-NS5A). Results: We estimated that 1.41 million patients would receive treatment with 2nd-generation DAAs from 2014 to 2020. Of these, 117,000 would fail to achieve SVR with DAAs, of which 58% are NS5A inhibitors failures (Figure 1). The characteristics of patients who fail on DAAs were: 51% cirrhosis, 72% GT1, 14% GT2, 9% GT3, and 5% GT4-6. Conclusions: Even in the era of highly efficacious DAAs, a

significant number of patients will fail to achieve SVR and will have limited re-treatment options. This population represents a group with significant unmet medical need. Safe and effective therapies are needed for this population to prevent the longterm sequelae of HCV. (Figure Presented).

Gastroenterology
Gill B, **Soman S**, and **Bhan A**. Comparison of the glasgow-blatchford risk score vs aims65 score in patients on coumadin and anti-platelet therapy or dual anti-platelet therapy *Am J Gastroenterol* 2016; 111:S494-S495. PMID: Not assigned. Abstract

B. Gill, Henry Ford Hospital, Detroit, United States

Introduction: Upper gastrointestinal bleeding (UGIB) risk stratification using validated prognostic scales can be used to provide appropriate management and give the clinician an indication of morbidity and mortality. The Glasgow-Blatchford Risk Score (GBRS) was developed to predict medical intervention needed, which included transfusion, endoscopy, or surgery. A higher GBS score also correlated with a higher likelihood of needing intervention. The AIMS65 Score has been validated to predict inpatient mortality in patients with UGIB. This particular study draws on these two prognostic tools and assesses their ability to risk stratify patients with UGIB on dual anti-platelet therapy (APA) or anti-platelet therapy (APA) with coumadin. Methods: This study was a retrospective study of 114 patients admitted to a tertiary care center with a primary diagnosis of UGIB from November 2013 to September 2015. Selected patients were on 2 APAs or APA and Coumadin at time of admission. The AIMS65 score was compared to the GBRS in predicting upper GI bleeding outcomes as it relates to 30 day readmission rates, mortality, re-bleeding, and intensive care unit (ICU) transfer amongst those on dual APAs or APA(s) with coumadin. The scores were compared using the area under the receiver operator curve (AUROC) with Statistical Analysis System software. Results: The GBRS correlated with a higher likelihood of ICU admission than the AIMS65 score. The two scores did not differ statistically between 30 day readmission rates, mortality, or re-bleeding. Conclusion: Patients presenting with UGIB, currently on dual APA regimen or APA with coumadin should be risk stratified with the GBRS in order to assess their need for ICU admission. Application of these findings may improve utilization of resources and facilitate clinical decision making in this subset of high risk patients.

Gastroenterology
Gonzalez HC, **Jafri SM**, and **Gordon SC**. Management of acute hepatotoxicity including medical agents and liver support systems *Clin Liver Dis* 2017; 21(1):163-180. PMID: 27842770. Full Text

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Drug-induced liver injury (DILI) can be predictable or idiosyncratic and has an estimated incidence of approximately 20 cases per 100,000 persons per year. DILI is a common cause of acute liver failure in the United States. No accurate tests for diagnosing DILI exist, and its diagnosis is based on exclusion of other conditions. Managing DILI includes discontinuing the suspected causative agent and in selected cases administering an antidote. Liver support systems are used for long-term support or as a bridge to transplantation and are effective for improving encephalopathy, hyperbilirubinemia, and other liver-related conditions, but whether they improve survival remains uncertain.

Gastroenterology
Gordon SC, Ahmed A, Kugelmas M, Dieterich DT, Wong R, **Brown KA**, Saab S, and Younossi ZM. A Decision analytic markov model to evaluate the health outcomes of sofosbuvir/velpatasvir for patients with chronic hepatitis C virus genotype 2 and 3 infection in the US *Hepatology* 2016; 63(1):422A-423A. PMID: Not assigned. Abstract

S.C. Gordon, Henry Ford Hospital, Detroit, United States

BACKGROUND AND AIM: The new oral single tablet regimen sofosbuvir / velpatasvir (SOF/VEL) has shown excellent efficacy and safety in patients with hepatitis C virus (HCV) genotypes (GT) 2 and 3. In particular, GT3 patients are considered difficult-to-treat populations with limited treatment options. A decision-analytic Markov model evaluated health outcomes with SOF/VEL in GT2 and 3 compared with current recommended alternatives with high

real-world utilization. METHODS: The analysis modeled cohorts of 10,000 chronic HCV GT2 or GT3 patients with a mean age of 52 years from a US third-party payer perspective over a lifetime horizon. 15% and 21% were cirrhotic (CC) and 10% and 40% were treatment-experienced (TE) in GT2 and GT3, respectively. In GT2, SOF/VEL was compared to SOF+ribavirin (R) and no treatment (NT); in GT3, SOF/VEL was compared to SOF+daclatasvir (DCV)+/-R and NT. Sustained virologic response (SVR) rates were based on Phase III clinical trials. Transition probabilities and utilities were based on a literature review and consensus by a panel of hepatologists. RESULTS: The SOF/VEL regimen resulted in the best health outcomes in terms of the lowest numbers of decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), and liver transplants (LT) when compared with all other comparators (Table 1). Results were consistent across patient subpopulations, including treatment naïve, pegintereron+ribavirin-TE, SOF+R-TE, non-cirrhotics, and cirrhotics. CONCLUSION These results demonstrate that SOF/VEL is highly effective in HCV GT2 and GT3 patients, leading to the fewest cases of liver-related complications vs. SOF+R and SOF+DCV. Furthermore, SOF/VEL provides a RBV-free option for GT2 and GT3, and is the only available pan-genotypic, all-oral, once-daily single tablet regimen for chronic HCV, simplifying treatment across GTs. Although studies report that efficacy and adherence rates for all-oral single tablet regimens are similar in real-world and clinical trial settings, additional analyses are necessary to determine the impact of real-world utilization (Table Presented).

Gastroenterology

Hart BR, **El Atrache M**, and **Zalawadia A**. A rare case of simultaneous metastatic disease of renal cell carcinoma to the stomach, bone, and lungs *Am J Gastroenterol* 2016; 111:S1143-S1144. PMID: Not assigned. Abstract

B.R. Hart, Henry Ford Hospital, Grosse Ile, United States

79 year old male patient with past medical history of stage 4 renal cell carcinoma status post nephrectomy and radiation presented with melena. His vital signs were normal upon presentation. Physical exam was unremarkable except for mild left sided abdominal pain without guarding or rebound. He was found to have a hemoglobin of 5.9g/dL from a baseline of 9g/dL, 2 months ago. Upper endoscopy showed a non bleeding non ulcerated vessel in the second portion of the duodenal bulb. This was consistent with a Dieulafoy's lesion (figure 1). It was treated with epinephrine injection and one hemoclip. In stomach we noted two ulcerated friable masses (3 cm and 4 cm). Biopsy showed Clear Cell carcinoma consistent with renal origin. Antral biopsy was remarkable for gastritis with reactive changes and H. pylori positivity. Imaging was performed to rule out further metastatic disease. CT showed numerous pulmonary metastatic nodules, a lesion in the right kidney, a lesion in the acetabulum with large destructive metastasis, and multiple abdominal lymph nodes and small enhancing peritoneal nodules with concern for metastatic disease. The patient was discharged to rehabilitation in a stable condition with appropriate outpatient follow up. Three weeks later he returned with hypoxia and was found to have a pulmonary embolus initially treated with Enoxaparin however he again developed melena, requiring 2 units pRBCs and was discharged to rehab. Seventeen days later he returned with additional GI bleeding with Hb of 7.2g/dL requiring 2 uPRBCs and was enrolled in hospice care. Renal cell carcinoma can metastasize to multiple organs. The most common sites are the liver, brain, bones, and lung. Metastatic disease to the stomach is very rare (0.2-4%). Our patient had metastatic disease in both of these organs as well as bone and lungs. This shows that RCC remains unpredictable in its pattern of spread. Oncologists should anticipate any pattern of presentation of RCC metastasis, and this report emphasizes the importance of close follow-up and a high suspicion for odd areas of metastasis. (Table Presented) (Figure Presented).

Gastroenterology

Hart BR, **Sedki M**, **Bukannan A**, **Zalawadia A**, **Blumenkehl M**, and **Jafri SM**. Retrospective analysis of specific vs non-specific beta blockers for variceal bleed *Am J Gastroenterol* 2016; 111:S1262-S1264. PMID: Not assigned. Abstract

B.R. Hart, Henry Ford Hospital, Grosse Ile, United States

Introduction: The most feared complication of cirrhosis is variceal bleeding with a high mortality (15 to 30%). Prophylactic treatment for variceal bleeds consists of treatment with nonselective beta blocker therapy (NSBB) or endoscopic variceal ligation. With reports of effective alternative BB therapy, this study aims to compare the efficacy of B2BB and NSBB therapy in cirrhotic patients with varices. Methods: An IRB approved retrospective study of 150 patients with cirrhotic patients with varices who were evaluated between 2003 and 2013 underwent chart review. One patient was excluded due to prior variceal bleed. The remaining 149 patients were evaluated from the initial EGD for subsequent bleeding, transplantation, or death. Medical therapy was evaluated. Descriptive statistics, Chi squared tests, and Kaplan-Meier Survival and Cox Regression curves were analyzed. Results: The population was 104/149 (69%) male with viral hepatitis the predominant cause of cirrhosis. 35 of 149 (24%) patients bled and 10 (6.7%) patients rebled. Other demographic data is shown in Table 1. Kaplan Meier analysis indicated no difference between individual BB therapy however results revealed Propranolol and No BB treatment had the longest time to bleed

Figure 1 where as “other” treatment was significantly different from no treatment, Propranolol and Metoprolol $p < 0.05$ table 2. Cox regession analysis revealed Metoprolol and Propranolol had significant effects on the model for bleeding risk $p < 0.05$ and for death Metoprolol was also significant. Other significant factors were varix size, MELD, and diuretic use $p < 0.05$. Conclusion: BB therapy for prevention of variceal bleeds has been shown to be effective in cirrhotic patients with high risk for variceal bleed. Our study aimed to try to address the role for B2BB. Our data revealed few statistical differences between BB therapies however suggested Metoprolol and Propranolol may play significant beneficial roles though with HR favoring the effect of propranolol. While not significant the trend suggests that propranolol may be the optimal BB. Current literature reveals similar findings favoring no BB treatment in the patients with low risk of bleed, while advantageous in patients with high bleeding risk. Further study is needed to elucidate the role of non selective BB within these populations. (Table Presented).

Gastroenterology

Kothari S, Thakkar S, **Rao B**, Kothari T, Garg MS, and Kaul V. Multimodal treatment approach for migrated and epithelialized metal biliary stents *Am J Gastroenterol* 2016; 111:S183. PMID: Not assigned. Abstract

S. Kothari, University of Rochester Medical Center, Strong Memorial Hospital, Rochester, United States

Introduction: Self-expandable metal stents (SEMS) are commonly placed for the palliation of obstruction due to pancreaticobiliary malignancies. Duration of patency ranges from six months to just under one year. Oncologic advancements may lead to survival beyond expected stent patency. Complications may arise including migration and epithelialization. We aim to highlight modalities available to successfully manage these complications. Methods We review multimodal approaches used to manage three cases of SEMS that were complicated by migration with and without epithelialization. All three patients had a history of pancreatic cancer and biliary obstruction with SEMS in place for a prolonged period ranging from months to years. Results Three cases demonstrate the use of Argon Plasma Coagulation(APC) and endoscopic scissors in the management of migrated and epithelialized biliary SEMS. These stents were trimmed using APC. APC settings ranged from 65 to 100watts, effect 1 with 1-1.4 Liters per min flow. Endoscissors were selectively used to manage embedding of metal meshwork. Symptoms related to stent migration and epithelialization resolved with endoscopic therapy. All patients tolerated procedures well and there were no complications in any of the cases. Conclusion: SEMS are often used for the palliation of malignant biliary obstruction. Migration along with significant epithelialization may occur with indwelling SEMS over prolonged periods of time. Multimodal treatment approaches that include APC and endoscopy scissors are safe and effective in the management of this complication.

Gastroenterology

Lee-Allen J, **Hussain S**, **Jones D**, **Jafri SM**, and **Siddiqui Y**. Meckel's diverticulum; an obscure cause of adult gastrointestinal bleed *Am J Gastroenterol* 2016; 111:S1371. PMID: Not assigned. Abstract

J. Lee-Allen, Ohio State University, Wexner Medical Center, Columbus, United States

Introduction: Meckel's diverticulum (MD) is a rare diagnosis for gastrointestinal bleeds for children and even rarer for teenagers and adults. It has a prevalence of only 2%. We describe the case of a young adult who had an unusual presentation for MD and prolonged work up eventually leading up to this frequently over-looked diagnosis. Case: A 21-year-old male presented to clinic with 2 episodes of painless melena. He had a previous episode of melena 3 years ago, with hemoglobin (Hgb) drop to 9g/dL for which he required transfusion. He was evaluated with a negative CT abdomen/pelvis, tagged RBC scan and meckel's scan. A small bowel follow through showed possible polypoid lesions of the ileum. Colonoscopy was poor prep but with polyps of ascending colon. The patient's vital signs were positive for orthostatic tachycardia. He reported occasional heartburn, self-treated with tums and milk without history of NSAID or alcohol use His labs were within normal limits, including a Hgb of 16.1. FOBT was positive. EGD was negative while colonoscopy was positive for limited visualization of smooth, polypoid mass in the transverse colon and multiple hypo-pigmented macules in the ascending colon. Biopsies were remarkable only for colonic mucosa with lymphoid aggregates. CT enterography (CTE) showed a hypervascular polypoid mass within the proximal ileum measuring 2.7 x 2.5 x 2.0 cm. The patient underwent single balloon enteroscopy to evaluate this area without success. Repeat colonoscopy was unrevealing. A recommendation for surgical consultation was made. The patient underwent laparoscopic, small bowel resection of a 2.5 x 2.5 x 1.0 cm polypoid mass thereafter. Pathology revealed heterotrophic, gastric mucosa consistent with a primary diagnosis of MD. Discussion: Bleeding from a MD can potentially occur at any age. These present typically with hematochezia and drop in Hgb. Approximately 10%-60% of these diverticula contain ectopic mucosa: most commonly gastric but also pancreatic or duodenal. Meckel's scan has a truncated predictive value and poor contribution in clinical decision-making. Laparoscopy is an effective diagnostic and therapeutic tool. Conclusion: This case highlights the importance of having a high index of suspicion for MD in

obscure GI bleed in younger patients recognizing the low sensitivity of a meckel's scan, limitation of endoscopic diagnostics as well as the diagnostic and therapeutic value of surgery.

Gastroenterology

Lenhart A, **Fernandez-Castillo J**, **Mullins K**, and **Salgia R**. A rare case of gastric variceal hemorrhage secondary to infiltrative b-cell lymphoma *Case Rep Gastroenterol* 2016; 10(3):518-524. PMID: 27843428. Full Text

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Portal hypertension commonly arises in the setting of advanced liver cirrhosis and is the consequence of increased resistance within the portal vasculature. Less commonly, left-sided noncirrhotic portal hypertension can develop in a patient secondary to isolated obstruction of the splenic vein. We present a rare case of left-sided portal hypertension and isolated gastric varices in a patient with large B-cell lymphoma, who was treated with splenic artery embolization. The patient is a 73-year-old male with no previous history of liver disease, who presented with coffee ground emesis and melena. On admission to hospital, he was found to have a hemoglobin level of 3.4 g/l. Emergent esophagogastroduodenoscopy showed isolated bleeding gastric varices (IGV1 by Sarin classification) in the fundus and cardia with subsequent argon plasma coagulation injection. He was transferred to our tertiary center where work-up revealed normal liver function tests, and abdominal ultrasound showed patent hepatic/portal vasculature without cirrhosis. MRI demonstrated a large heterogeneously enhancing mass in the pancreatic tail, with invasion into the spleen and associated splenic vein thrombosis. Surgery consultation was obtained, but urgent splenectomy was not recommended. The patient instead underwent splenic artery embolization to prevent future bleeding from his known gastric varices. Pathology from a CT-guided biopsy was consistent with diffuse large B-cell lymphoma. PET imaging showed uptake in the splenic hilum/pancreatic tail region with no additional metastatic involvement. He was evaluated by the Hematology Department to initiate R-CHOP chemotherapy. During his outpatient follow-up, he reported no further episodes of melena or hematemesis. To the best of our knowledge, there have only been two published case reports of large B-cell lymphoma causing upper gastrointestinal bleeding from isolated gastric varices. These cases were treated with splenectomy or chemotherapy alone. Thus far, splenectomy has been the standard treatment approach for splenic vein thrombosis with clinical complication, such as gastric variceal bleeding. We present a case of successful treatment of bleeding isolated gastric varices using a less invasive and less morbid approach through splenic artery embolization. This case highlights the need for an increased awareness of the diverse etiologies of left-sided portal hypertension and isolated gastric varices, as well as the consideration of minimally invasive management strategies.

Gastroenterology

Lenhart A, **Folt D**, **Markus J**, **Cerasale M**, and **Moonka D**. A rare case of a sex cord stromal tumor presenting as elevated liver function tests *Am J Gastroenterol* 2016; 111:S864-S865. PMID: Not assigned. Abstract

A. Lenhart, Henry Ford Hospital, Detroit, United States

Liver metastases are far more common than primary liver carcinoma, with the most common primary malignancies arising from the colon, rectum, breast, and lung. Sex cord tumors, on the other hand, do not commonly metastasize to the liver, and rather present with pelvic pain or signs of estrogen or androgen excess. We present a rare case of a sex cord stromal tumor manifesting as right upper quadrant (RUQ) pain and elevated liver function tests (LFTs). The patient is a 28-year-old female, G2P1001, who was 20 weeks pregnant at the time of admission, who presented with a several week history of RUQ abdominal pain. She denied any fevers, vomiting, or diarrhea. However, she did report around a ten-pound weight loss since the start of her pregnancy. Upon arrival, her LFTs were elevated: ALT 199, AST 92, ALP 493, T Bilirubin 1.6, D Bilirubin 0.9. Ultrasound revealed dilation of the common bile duct (CBD) to 13.5 mm along with intrahepatic biliary dilation. Gastroenterology was consulted and she underwent endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy. No stones were present, but the major papilla was edematous with oozing and inflammation, consistent with the recent passage of a CBD stone. She underwent magnetic resonance imaging and magnetic resonance cholangiopancreatography, which were negative for choledocholithiasis and portal vein thrombosis. However, the morphology of the liver appeared abnormal, suggesting hepatic nodularity and heterogeneity (Figure 1). Given persistent symptoms, she underwent cholecystectomy with liver biopsy. Of note, the liver also appeared nodular intra-operatively (Figure 2). Surprisingly, liver pathology was consistent with a malignant epithelioid neoplasm, likely a sex cord stromal tumor. AFP was elevated at 53.6 ng/mL. Oncology was consulted and recommended additional imaging of her ovaries with pelvic ultrasound. Her case is to be discussed at an upcoming Tumor Board meeting to evaluate for treatment options. Malignant sex cord stromal tumors are rare, and only comprise around 1-2% of ovarian neoplasms. Metastasis is also uncommon, but typically the tumors will spread regionally to the diaphragm or omentum. Metastasis to the liver is exceedingly rare, and

literature on the topic, including treatment options in pregnancy is limited. This case illustrates a unique presentation of metastatic disease to the liver and highlights the importance of tissue diagnosis in atypical presentations of hepatic disease. (Figure presented).

Gastroenterology
Lenhart A, **Hassan M**, **Meighani A**, **Sadiq O**, and **Siddiqui Y**. A perplexing case of abdominal pain that led to the diagnosis of zollinger-ellison syndrome *Am J Gastroenterol* 2016; 111:S1056. PMID: Not assigned. Abstract

A. Lenhart, Henry Ford Hospital, Detroit, United States

Zollinger-Ellison Syndrome (ZES) is a rare clinical disorder, characterized by hypersecretion of gastric acid and multiple ulcers distal to the duodenal bulb. This occurs via the release of gastrin by neuroendocrine tumors known as gastrinomas. Patients with ZES present with nonspecific GI symptoms, which often leads to a delay in diagnosis. We present a case that highlights the importance of increased awareness of ZES in patients with chronic GI complaints. The patient is a 55 year-old female with a history of chronic pancreatitis, who had been following in the GI clinic for several years, secondary to abdominal pain, nausea, and diarrhea. However, despite extensive testing, an etiology of her symptoms had not been determined. She initially underwent esophagogastroduodenoscopy (EGD) and endoscopic ultrasound (EUS), which only showed gastropathy and chronic pancreatitis. Magnetic resonance cholangiopancreatography was unremarkable. She underwent cholecystectomy, but continued to have symptoms, which prompted a repeat EGD. This showed a deep ulceration at the gastro-esophageal junction (LA Grade D), a 2 cm deeply cratered ulcer in the second portion of the duodenum, and a stricture in the third portion of the duodenum (Figure 1). Biopsies showed gastritis and duodenitis without evidence of malignancy. These findings were suspicious for ZES, and work up was initiated. Serum gastrin level was elevated at 1639 pg/mL, but repeat EUS and CT abdomen/pelvis did not reveal any pancreatic or duodenal masses. Somatostain receptor scintigraphy (SRS) was obtained, which showed two small lesions in the gastrinoma triangle (Figure 2). She subsequently underwent a Whipple pancreaticoduodenectomy. Pathology was positive for four microscopic foci (largest 0.1 cm) of a well-differentiated neuroendocrine tumor with evidence of metastasis to two peri-pancreatic nodes. She reported improvement in her symptoms after surgery. This case highlights the need for increased awareness of ZES in patients with unexplained GI complaints. The time to diagnosis in this patient was over seven years, which may have been reduced if ZES was considered earlier. This case also emphasizes the use of multiple modalities in the diagnosis of ZES. SRS, which ultimately detected the gastrinoma in this patient, has a higher sensitivity than CT/MRI. EUS also has a high sensitivity; however, a pancreatic mass was not identified with EUS in our patient, possibly secondary to the small size of the tumor. (Figure Presented).

Gastroenterology
Li J, **Gordon SC**, **Rupp LB**, **Zhang T**, **Trudeau S**, Holmberg SD, Moorman AC, Spradling PR, Teshale EH, Boscarino JA, Daida YG, Schmidt MA, and **Lu M**. Long-term progression of viral load and serum markers of fibrosis among treated and untreated patients with chronic hepatitis B *J Gastroenterol Hepatol* 2016;PMID: 27888529.
Full Text

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BACKGROUND AND AIMS: Antiviral therapy for patients with hepatitis B (HBV) infection is generally deferred for "immune inactive" patients, although longitudinal changes in viral load and liver fibrosis remain understudied in this population. Likewise, in treated patients, the temporal relationship between changes in viral load and liver fibrosis is not well-characterized. Using data from the Chronic Hepatitis Cohort Study, we investigated viral load and the Fibrosis-4 index (FIB4, a serum-based marker of liver fibrosis) trajectories in both untreated and treated HBV patients. MATERIALS AND METHODS: We applied a bivariate, piecewise, linear spline, mixed-effects modeling approach to data from 766 HBV patients (342 untreated, 424 treated). Treatment selection bias was adjusted using propensity scores. Multiple sensitivity analyses were used to confirm results in untreated patients. RESULTS: Among all untreated patients, FIB4 began to increase by 0.9% per month (11% per year) ($p < 0.05$) at 28 months post-index date, suggesting fibrosis progression. Significant FIB4 progression was also observed within a subgroup analysis of "immune inactive" untreated patients. In treated patients, viral load declined 31.8% per month ($p < 0.05$) for the first 5

months after treatment initiation, and 1.4-1.7% per month ($p < 0.05$) thereafter. At 5 months after treatment initiation, FIB4 began to decline 0.5% per month ($p < 0.05$), stabilizing at 28 months. CONCLUSION: Among untreated HBV patients, FIB4 gradually increases over time, suggesting fibrosis progression, even in those patients designated as immune inactive. In treated patients, antiviral therapy results in a rapid decline in viral load followed by a delayed decline in markers of liver fibrosis.

Gastroenterology
Lu M, **Gordon SC**, **Li J**, **Rupp LB**, **Zhou Y**, Moorman AC, Spradling P, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, **Trudeau S**, and Holmberg SD. Hepatitis C complications: Prevalence and disparities in a large US cohort 2006-2014 *Hepatology* 2016; 63(1):95A-96A. PMID: Not assigned. Abstract

M. Lu, Public Health Science, Henry Ford Health System, Detroit, United States

The burden of hepatitis C virus (HCV)-related cirrhosis, decompensated cirrhosis, and mortality has not been well-described in a large "real world" US population. We investigated trends in the prevalence of cirrhosis and decompensated cirrhosis, and incidence of mortality, among HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS) from 2006-2014. Methods: CHeCS is a longitudinal observational study of hepatitis patients from 4 large US health systems. Cirrhosis was ascertained using ICD9 codes, liver biopsy reports, and serum markers of fibrosis. Decompensated cirrhosis was ascertained using a set of ICD9 codes that have been validated as predictive of decompensated cirrhosis. We used join-point modeling (univariate and multivariate) to identify rates of change in prevalence over time as well as "break points" that indicate different phases of Annual Percentage Change (APC). Results: Of 11,286 adult HCV-infected patients, prevalence of cirrhosis increased from 10% in 2006 to 28% in 2014. Join-point analysis identified a breakpoint at 2007, with adjusted APCs of 49.1 (2006-2007; $p<0.05$) and 9.5 (2007-2014; $p<0.05$). Prevalence of decompensated cirrhosis increased from 3% in 2006 to 7% in 2014, with two breakpoints (at 2008 and 2012) and three segments, with APCs of 25.9 (2006-2008; $p<0.05$), 8.7 (2008-2012; $p<0.05$), and 1.4 (2012-2014). Incidence of all-cause mortality increased from 1.1% in 2006 to 3.1% in 2013, with a breakpoint in 2010 and APCs of 20.0 (2006-2010; $p<0.05$) and 4.2 (2010-2013). Older patients, Asian/Pacific Islanders, and men all demonstrated higher prevalence of cirrhosis and decompensated cirrhosis. Black patients demonstrated the highest incidence of all-cause mortality. Conclusions: Over the past decade, prevalence of cirrhosis among HCV patients in this US cohort increased almost 3-fold. During the same time period, prevalence of decompensated cirrhosis and incidence of all-cause mortality more than doubled, although the increase in both plateaued in recent years (Figure Presented).

Gastroenterology
Lu M, **Li J**, **Rupp LB**, Boscarino JA, Raebel M, Schmidt MA, Haller IV, Daida Y, Rodriguez CV, Sahota A, VanWormer JJ, Romanelli RG, Vincent J, and **Gordon SC**. Prevalence of primary biliary cholangitis (PBC) in large US health care systems: Case ascertainment using electronic health records *Hepatology* 2016; 63(1):196A. PMID: Not assigned. Abstract

M. Lu, Public Health Science, Henry Ford Health System, Detroit, United States

There is little data on the prevalence of primary biliary cholangitis (PBC) in the US. Estimates of prevalence vary widely- from 1.91 to 40.2 per 100,000 persons-depending on the rigor of the method used. We developed a method to ascertain PBC cases using electronic health record (EHR) data and report PBC prevalence among patients receiving care at one of 11 US health systems associated with the Fibrotic Liver Disease (FOLD) Consortium. Methods: We used broad initial EHR inclusion criteria (positive/abnormal anti-mitochondrial antibody test [AMA]; ICD-9 diagnosis code for PBC [571.6]; or receipt of the drug ursodeoxycholic acid) to ensure capture of all possible PBC cases. Chart review was conducted to confirm PBC in a random sample of patients, stratified by likelihood of PBC and year of diagnosis. Next, a Classification and Regression Tree (CART) model, starting with 15 EHR-based variables, was developed using a learning sample. The optimized PBC CART model was validated using 20-fold cross-validation. Overall prevalence was estimated using CART-identified PBC patients as the numerator, and number of patients receiving care (defined as either ≥1 or ≥2 encounters with participating health systems from 2003-2014) as the denominator. Results: Among 1.4 million patients seen at FOLD health systems between 2003 and 2014, 3711 met at least one initial inclusion criterion; 421 of these were selected for chart review. A CART model with five variables (AMA positive, PBC ICD-9 diagnosis code, alkaline phosphatase >120 IU/L, sex, and age) achieved optimal classification (area under the receiver operator characteristic curve: 0.94 for the learning sample; 0.90 using 20-fold cross-validation). Validation results had specificity=0.90; sensitivity= 0.90; positive predictive value (PPV)=0.83; and negative predictive value (NPV)=0.94. In a subset of 183 recent patients who met one of the initial inclusion criteria during 2010-2014, results showed specificity=0.95; sensitivity=0.82; PPV=0.85; and NPV=0.94. Application of the CART algorithm to all 3711 patients who met at least one initial inclusion criteria identified 589 PBC

patients. Twelve-year period prevalence was 41.8 or 41.6 per 100,000, based on either ≥1 or ≥2 heath system encounters. The ratio of women to men was 9:2. Conclusions: An algorithm applied to EHR data can efficiently and accurately identify patients with PBC. Chart review at the ten remaining FOLD sites will be used to validate the algorithm; PBC prevalence will then be determined across the Consortium. Given the rarity of PBC, leveraging automated EHR-based identification could facilitate research into this serious autoimmune condition.

Gastroenterology
Meighani A, **Hassan M**, **Lenhart A**, and **Gordon S**. Aortitis in a patient with chronic hepatitis C virus infection *Am J Gastroenterol* 2016; 111:S870-S871. PMID: Not assigned. Abstract

A. Meighani, Henry Ford Hospital, Detroit, United States

Chronic hepatitis C virus (HCV) infection is a recognized cause of cryoglobulinemic vasculitis. It is an immune-complex mediated systemic inflammatory syndrome that generally involves small-to-medium sized vessels. Aortitis and other large vessel vasculitides secondary to cryoglobulinemia are very rare and are seldom reported. We report a case of a 70-year old Caucasian male with a past medical history of gout and untreated non-cirrhotic chronic HCV, genotype 1a, who presented with a one-week history of moderately severe, right-sided abdominal pain. He also reported a two-week history of a non-blanching, erythematous, maculo-papular rash on his trunk and back, which was partially relieved by a corticosteroid cream. His work up in the Emergency Department included a CBC that showed leukocytosis of 14 K/uL and a computed tomography (CT) scan of his abdomen with contrast, which showed inflammatory changes near the bifurcation of the aorta. This prompted a CT angiography (CTA) that showed diffuse wall thickening of the distal abdominal aorta and common iliac vessels without evidence of contrast extravasation (Figures 1-2), findings that were suggestive of a focal, large vessel vasculitis. Laboratory studies showed C-reactive protein and erythrocyte sedimentation rate elevated to 8.7 mg/dL and 34 mm/hr, respectively. Rapid plasma reagin test for syphilis was negative. The HCV RNA was 183, 424 IU. Serum for cryoglobulins was positive. The decision was subsequently made to initiate simultaneous treatment with ledipasvir/sofosbuvir as well as oral prednisone of 20 mg daily which was tapered off over 3 months. He completed a total of 12 weeks of therapy and ultimately achieved a sustained virologic response. A follow up magnetic resonance angiography (MRA) was performed four months after his initial presentation, and showed resolution of the previously noted distal abdominal aorta, bilateral common iliac arteries, and proximal bilateral external iliac artery wall thickening (Figure. 3). His CRP and ESR also improved within a month of starting treatment. This case highlights a previously unreported example of large vessel cryoglobulinemic vasculitis involving the distal aorta, presumably mediated by HCV infection. The rapid improvement following initiation of sofosbuvir/ledipasvir emphasizes the need to search for viral etiology in similar cases and to promptly begin potentially lifesaving therapy. (Figure presented).

Gastroenterology
Meighani A, **Ramesh M**, and **Salgia R**. Successful outcomes of fecal microbiota transplantation in patients with chronic liver disease *Hepatology* 2016; 63(1):1016A-1017A. PMID: Not assigned. Abstract

A. Meighani, Internal Medicine, Henry Ford Hospital, Detroit, United States

Background: Fecal Microbiota Transplantation (FMT) has been shown to be a promising treatment option for patients with recurrent and/ or refractory Clostridium Difficile Infection (CDI). Despite increasing research on FMT, little is known about outcomes in patients with liver disease or cirrhosis. We aimed to study the outcomes of FMT in patients with chronic liver disease (CLD) at our tertiary medical center. Methods: A cohort of all patients who had undergone FMT from December 2012 to May 2014 for refractory or recurrent CDI was identified. Patients were followed up for 1 year post-FMT. Response to treatment was defined as resolution of symptoms in 7 days. Severe CDI was defined as a rise in creatinine >1.5 times above baseline, WBC ≥ 15,000 cells/mL, or albumin < 1.5 g/ dl within 2 weeks of symptom onset. Descriptive analysis was performed to determine the outcomes of FMT in patients with CLD as compared to the comparison cohort without liver disease. Results: A total of 201 patients underwent FMT for CDI, from which 14 had a history of chronic liver disease. Nine of these patients had cirrhosis with a mean Child-Turcotte-Pugh (CTP) score of 8. One patient was 5 months post-liver transplant at the time of FMT. Mean age of patients in the liver disease cohort was 62 with 71% being female. Recent antibiotic use was a common risk factor related to CDI development and was found to be significantly different between both groups (17% of CLD patients vs 58% in the general cohort, p= 0.01). Although some patients were immunosuppressed due to history of IBD or liver transplant, there was no significant difference between the two groups and their outcomes in terms of immunosuppression, route of FMT delivery, number of CDI infections within the prior 3 months, recent hospitalization, recent surgeries or Charlson comorbidity index. There was no significant difference in the number of patients with severe grading of CDI among patients with CLD and the general cohort (36% vs 24%, p= 0.34). Four patients with CLD received >1 FMT, of which 2 remained non-responders. Overall, there was no significant difference in FMT response between patients

with liver disease and the rest of the cohort (12/14, 87% vs 164/187, 88%, p= 0.68). Both patients who failed FMT in the CLD cohort had decompensated cirrhosis with CTP scores of 9 and 12, respectively. Conclusion: Fecal microbiota transplantation is a safe and successful treatment option for patients with recurrent and/or refractory CDI who have stable chronic liver disease or compensated cirrhosis. Recent antibiotic use was less commonly a risk factor for CDI in patients with liver disease.

Gastroenterology
Meighani A, **Rao B**, **Hassan M**, **Abboud R**, and **Pompa R**. Does presenting with an acute diverticular bleed prior to the weekend result in a longer wait time to colonoscopy? *Am J Gastroenterol* 2016; 111:S1227-S1228. PMID: Not assigned. Abstract

A. Meighani, Henry Ford Hospital, Detroit, United States

Introduction: We aimed to see if patients admitted for diverticular bleeding who presented to the hospital just prior to the weekend (Friday) were less likely to receive an early colonoscopy compared to all other days of the week. Methods: Retrospective chart review of 573 patients with a diagnosis of diverticular bleeding was done between May 2013 and May 2015 at a large urban tertiary care center and its associated satellite hospitals. Patients were included for analysis only if they were admitted to the hospital and had a colonoscopy performed while inpatient. Data was obtained on patient demographics, day of presentation with a lower GI bleed, day of colonoscopy and time of colonoscopy. Time of colonoscopy was defined as early (performed less than 24 hours from presentation to the emergency department) and late (24 or more hours). A 2x2 contingency table was used to calculate statistics. Results: 297 patients met inclusion for analysis. Mean age was 76.3 with 56.9% being females and 61.6% African American. The majority of patients (78.1%) had a late colonoscopy performed irrespective of the day of presentation (Table I). Of those presenting on Friday 10.9% received an early colonoscopy versus 23.9% for all other days of the week ($p = 0.0493$). Conclusion: Our studied population shows that most patients underwent colonoscopy after 24 hours from initial presentation. Those presenting just prior to the weekend were even less likely to receive an early colonoscopy compared to all other days of the week. (Table Presented).

Gastroenterology
Moonka D, **Nagai S**, **Divine G**, and **Salgia R**. Influence of donor age and cold ischemia on recurrence of hepatocellular carcinoma after liver transplantation *Transplantation* 2016; 100(7):S427. PMID: Not assigned. Abstract

D. Moonka, Gastroenterology and Hepatology, Henry Ford Health System, Detroit, United States

Introduction: The role of donor age on recurrence of hepatocellular carcinoma (HCC) after liver transplant (LT) is not clear. In the current analysis, we evaluate the impact of donor age and cold ischemia time on HCC recurrence after LT. Methods: We evaluated 303 consecutive LT patients at our institution with HCC. Nine were excluded because of findings of cholangiocarcinoma, 11 were excluded because of death within three months and one because of positive HCC margins at LT leaving 282 patients. . Patients were evaluated for a variety of factors for association with time to HCC recurrence using Kaplan-Meier estimates and logrank tests. Multivariate modeling was done using Cox regression analysis. Results and Discussion: In the 282 patients, there were 41 HCC recurrences (14.5%) occurring at a median of 17 months and a mean of 22.2 months and a range of 22 to 98 months. On univariate analysis, factors associated with HCC recurrence were cold ischemia ($P < 0.001$), donor age ($P=0.025$), tumor burden within Milan criteria on explant ($P < 0.001$), maximum alpha-fetoprotein (AFP) ($P=0.005$) and AFP at time of LT ($P < 0.001$), poorly differentiated histology ($P < 0.001$), vascular invasion ($P < 0.001$) and percent necrosis ($P=0.017$) in those undergoing pre-LT treatment. Patients with HCC recurrence had a donor age of 47.0 ± 16.7 and those without had a donor age of 41.2 ± 16.2 ($P=0.038$). Patients with recurrence had a cold ischemia time in hours of 6.8 ± 2.1 vs 5.6 ± 1.7 in those without ($P=0.001$). For both donor age and cold ischemia, the Youden's J statistic was used to determine an optimal cutoff to discriminate between patients with and without recurrence. The 209 patients with donors less than 55 years old had 1, 3 and 5 year tumor free survival of 93.7%, 90.2% and 87.3% vs 91.5%, 78.4% and 70.3% in the 73 patients with donors over 55 ($P=0.009$). The 119 patients with cold ischemia less than 5.5 hours had 1, 3 and 5 year tumor free survival of 95.8%, 92.6% and 91.0% vs 91.2%, 82.7% and 76.6% in the 150 patients over 5.5 hours ($P=0.006$). The 37 patients with donors over 55 and cold ischemia over 5.5 hours had 1, 3 and 5 year tumor free survival of 88.7%, 67.0% and 57.4% vs 95.4%, 92.5%, and 92.5% for the 88 patients with both lower donor age and shorter cold ischemia. In a multivariate analysis controlling for tumor burden, histology and vascular invasion: donor age ($P=0.007$), cold ischemia ($P=0.005$), Milan criteria on explant ($P=0.002$), maximum AFP ($P=0.016$), AFP at OLT ($P=0.004$), poorly differentiated histology ($P < 0.001$) and vascular invasion ($P=0.002$) were associated with time to tumor recurrence Conclusions: Both lower donor age and shorter cold ischemia time were independently associated with improved tumor free survival after liver transplant. If confirmed in larger cohorts, these represent potentially modifiable factors in liver transplant patients with liver cancer.

Gastroenterology
Moonka D, **Nagai S**, **Gadde R**, **Datta L**, **Divine G**, **Abouljoud MS**, and **Salgia R**. Effect of tumor necrosis from loco-regional therapy prior to liver transplantation on hepatocellular carcinoma recurrence after transplant *Hepatology* 2016; 63(1):640A-641A. PMID: Not assigned. Abstract

D. Moonka, Division of Gastroenterology, Henry Ford Hospital, Detroit, United States

Few studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on recurrence of hepatocellular carcinoma (HCC) after LT. We describe results in 181 LT patients. Methods: We evaluated 260 consecutive LT patients with presumed HCC. Patients were excluded for cholangiocarcinoma (9), death within 3 months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients. Patients were evaluated for factors associated with time to HCC recurrence using Kaplan-Meier estimates with log-rank test. Multivariate modeling used Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had 1 treatment, 25 had 2 and 4 had 3 treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium-90 embo-lization. 30 patients had HCC recurrence at a mean of 24.0 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without (P=0.023). A cutoff of 85% necrosis gave a maximal Youden's J statistic for discriminating groups less likely to recur from those more likely. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For 114 patients with < 85% necrosis, 1, 3 and 5 year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant in part because all patients with > 85% necrosis were within Milan. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Gastroenterology
Moonka D, **Shah V**, **Datta L**, **Gadde R**, **Divine G**, **Yoshida A**, **Jafri SM**, and **Salgia R**. Degree of tumor necrosis from pre-transplant loco-regional therapy is associated with tumor free survival after liver transplantation *Transplantation* 2016; 100(7):S429. PMID: Not assigned. Abstract

D. Moonka, Gastroenterology and Hepatology, Henry Ford Health System, Detroit, United States

Introduction: Previous studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on the rate of recurrence of hepatocellular carcinoma (HCC) after transplant. These studies have shown mixed results. We describe our results in 181 LT patients with HCC at our center. Methods: We evaluated 260 consecutive LT patients at our institution with known HCC. Patients were excluded for cholangiocarcinoma (9), death within three months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients of whom 30 had HCC recurrence. Patients were evaluated for a variety of factors for association with time to HCC recurrence using Kaplan-Meier estimates and log-rank tests. Multivariate modeling was done using Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had one treatment, 25 had two and four patients had three treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium (Y-90) embolization. Thirty patients had HCC recurrence at a mean of 24.0 months with a range of 3.4 to 97.6 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without recurrence (P=0.023). A cutoff of 85% tumor necrosis gave the maximal Youden's J statistic for discriminating groups most likely to recur from those less likely to do so. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For the 114 patients with < 85% necrosis, 1, 3 and 5 year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant. Of note, all patients with > 85% necrosis were within Milan criteria on explant. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and

maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, the percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Gastroenterology
O'Leary JG, Fontana RJ, **Brown K**, Burton JR, Jr., Firpi-Morell R, Muir A, O'Brien C, Rabinovitz M, Reddy KR, Ryan R, Shprecher A, Villadiego S, Prabhakar A, and Brown RS, Jr. Efficacy and safety of simeprevir and sofosbuvir with and without ribavirin in subjects with recurrent genotype 1 hepatitis c post-orthotopic liver transplant: The randomized galaxy study *Transpl Int* 2016;PMID: 27896858. Full Text

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This prospective, randomized, phase 2 study in subjects with recurrent hepatitis C virus (HCV) genotype 1 post-orthotopic liver transplant evaluated once-daily simeprevir 150mg+sofosbuvir 400mg, with and without ribavirin 1,000mg. Primary endpoint was proportion of subjects with Week 12 sustained virologic response (SVR12). Thirty-three subjects without cirrhosis were randomized 1:1:1 into three arms (stratified by geno/subtype and Q80K): Arm 1, simeprevir+sofosbuvir+ribavirin, 12 weeks; Arm 2, simeprevir+sofosbuvir, 12 weeks; Arm 3, simeprevir+sofosbuvir, 24 weeks; 13 additional subjects (2 with cirrhosis, 11 without cirrhosis) entered Arm 3. All 46 subjects received at least one dose of study drug; median age, 60 years; 73.9% male; 80.4% white; 71.7% geno/subtype 1a (12 [36.4%] of these had Q80K); median 4.5 years post-transplant. Among randomized subjects, SVR12 was achieved by 81.8% in Arm 1, 100% in Arm 2, and 93.9% in Arm 3; two subjects did not achieve SVR12: one viral relapse (follow-up Week 4; Arm 1) and one missing follow-up Week 12 data. In total, five subjects had a serious adverse event, considered unrelated to treatment per investigator. Simeprevir exposure was increased relative to the non-transplant setting, but not considered clinically relevant. Simeprevir+sofosbuvir treatment, with or without ribavirin, was efficacious and well tolerated (ClinicalTrials. gov Identifier: NCT02165189) This article is protected by copyright. All rights reserved.

Gastroenterology
Parekh R, **Ramesh MS**, and **Tang J**. Lymphocytic colitis in patients with recurrent clostridium difficile colitis: Case series *Am J Gastroenterol* 2016; 111:S1308. PMID: Not assigned. Abstract

R. Parekh, Henry Ford Hospital, Detroit, United States

Introduction: Clostridium difficile (C.diff) has been associated with collagenous colitis in a few case reports. We present a case series of 3 patients with refractory C.diff infection treated with fecal microbiota transplantation (FMT) from healthy donors, who were eventually found to have lymphocytic colitis. Case 1 An 80-year-old female with had a bout of C.diff infection. Despite appropriate antibiotic treatment with 2 courses of oral metronidazole and vancomycin, she had recurrent episodes of diarrhea. She underwent FMT via enema twice, but neither transplant was effective. Colonoscopy showed only mild inflammation throughout the colon with no pseudomembranes and FMT was performed. Random biopsies were consistent with Lymphocytic Colitis (LC). She was treated with bismuth salicylate with complete resolution of symptoms. Case 2 A 44-year-old female had refractory C.diff infection that failed treatment with multiple (>6) courses of oral metronidazole and vancomycin. She underwent colonoscopy which showed mild erythema and pseudomembranes in the right colon. Random biopsies were consistent with LC. The patient was subsequently treated with budesonide which signifi- cant improvement in her diarrhea. She has been maintained on bismuth salicylate with loperamide as needed. Case 3 A 64-year-old male was admitted initially with C.diff colitis. He was treated with oral vancomycin and metronidazole with resolution of symptoms. He had recurrent symptoms requiring FMT via enema twice without resolution of his symptoms. He eventually underwent a colonoscopy that showed mild inflammation. Random biopsies were consistent with LC. He was treated with bismuth

salicylate with complete resolution of diarrhea. Discussion: We have discussed three cases who all had recurrent/refractory C.diff colitis who had persistent diarrhea in spite of FMT. All patients had random biopsies of colon positive for LC and had complete resolution of diarrhea with treatment of LC. The observation from this case series raises many questions that will require further research. Is LC is a consequence of recurrent C.diff colitis infection, the treatment or a concomitant entity leading to recurrent diarrhea? It is also unknown if the FMT from healthy donor plays a role in the development of LC We would like to highlight the importance of pursuing other causes of diarrhea like microscopic colitis in patients presenting with recurrent episodes of C.diff colitis in spite of treatment with FMT.

Gastroenterology
Ramesh MS, **Khanna S**, **Messer J**, and **Adams M**. Durable prevention of recurrent C. Difficile infection with RBX2660: Results of the PUNCH CD 2 trial *Am J Gastroenterol* 2016; 111:S93. PMID: Not assigned. Abstract

M.S. Ramesh, Henry Ford Hospital, Detroit, United States

Introduction: Antibiotic treatment of C. difficile infection (CDI) with standard of care antibiotics is associated with high recurrence rates. Microbiota-based drugs have shown promise in durable prevention of CDI recurrence.1 We report on the durability of RBX2660 for the prevention of recurrent CDI in in a post-hoc analysis of PUNCH CD 2, a Phase 2b a randomized, double-blinded, placebo-controlled trial. Methods: Patients enrolled in the PUNCH CD 2 trial were randomized to receive either: 2 doses of RBX2660 (a microbiota-based drug manufactured from live human-derived microbes); 2 doses of placebo; or 1 dose of RBX2660 and 1 dose of placebo via enema with doses 7 days apart. The placebo consisted of normal saline and cryoprotectant in the same proportions found in RBX2660. Success was measured as the absence of CDI symptoms at 8 weeks post treatment. Failures in any study group were eligible to receive open-label treatment with up to 2 doses of RBX2660. Failure was defined as recurrent C. difficile-associated diarrhea; positive CDI stool test; need for retreatment for CDI; no other cause for CDI symptoms. Patients will be followed to 24 months after completing the last treatment. Results: A total of 107 patients (median age 63, range: 18-92 years; 59.8% female) at 21 centers in the U.S. and Canada received at least 1 dose of RBX2660 with an overall success rate of 88.8% (95/107). Of these patients, 4.2% (4/95) developed a new episode of CDI confirmed by a positive test > 8 weeks after the last RBX2660 treatment. One episode occurred after the patient was treated with antibiotics for a dog bite; another during a hospital stay for small bowel obstruction; and 2 were of unknown origin. The long-term CDI-free rate (median follow-up: 8.3 months; range 1.6 to 14.9 months) was 95.8% (91/95), Table 1. The median time to a new CDI episode was 135, range: 61-259 days after treatment with RBX2660. Conclusion: Recurrent CDI poses on-going treatment challenges with high recurrence rates after standard antibiotic treatment. RBX2660, a microbiota-based drug, was demonstrated as an efficacious treatment for recurrent CDI with long-term durability in both open-label and randomized controlled trials. Long-term follow-up is ongoing. (Table presented).

Gastroenterology
Rao B, **Markus J**, **Bukannan A**, **Parekh R**, and **Moonka D**. Acute pulmonary embolism masquerading as acute liver failure *Am J Gastroenterol* 2016; 111:S946. PMID: Not assigned. Abstract

B. Rao, Henry Ford Hospital, Grand Blanc, United States

Introduction: A clinical presentation of acute liver failure (ALF) due to pulmonary embolism (PE) is rare with only one prior report to our knowledge. Case Presentation: 32 year-old Caucasian female presented with nausea, vomiting, and somnolence. She had Crohn's disease with recent adjustment of therapy for poorly controlled disease. She was on multiple home medications, recently completed amoxicillin for a tooth abscess, and did no excess acetaminophen use. She was afebrile with a heart rate of 109 beats per minute, blood pressure of 167/80 mmHg, and oxygen saturation of 82%. She was anicteric, without abdominal distention, and without notable lower extremity edema. She was not fully oriented and had asterixis. Her laboratory values revealed an elevated AST of 9616 IU/L, ALT of 2350 IU/L, and INR of 2.29. She had a leukocytosis of 13.7 K/uL, platelet count of 94 K/uL, and creatinine of 1.67 mg/dL. Viral and autoimmune labs were unrevealing. An ultrasound demonstrated increased liver echogenicity with patent vasculature. A chest x-ray showed a right upper lobe pneumonia and CT head did not show cerebral edema. Her findings were consistent with ALF with initial concern for possible drug induced liver injury (DILI). Initial management consisted of neurologic and hemodynamic monitoring, N-acetylcysteine, and antibiotics for pneumonia. Transplant evaluation was initiated which included a transthoracic echocardiogram (TTE) on the second day of admission. It revealed a severely enlarged right ventricle with reduced systolic function. A follow-up CT pulmonary angiogram revealed multiple large bilateral PE with significant clot burden and reflux of contrast into the hepatic veins. Anticoagulation was initiated with heparin. Her liver studies improved and normalized, her mental status changes resolved, and she did not require transplantation. Discussion: The patient's initial clinical presentation led to work-up for more common ALF etiologies with concern for DILI due to multiple medications along with recent amoxicillin. PE

may pose a diagnostic challenge as her tachycardia and hypoxia were initially attributed to pneumonia. Her TTE as part of a transplant evaluation was the initial clue to a PE diagnosis. Of mention, the patient did have IBD which is a known risk for venous thromboembolism. Although rare, an extensive PE leading to a presentation of ALF should be considered in the differential particularly for those with risk factors (Figure Presented).

Gastroenterology
Siddiqui MA, Eraqi H, **Omar S**, and **Jafri SM**. Massive disparity in insurance approval; a comparison between ledipasvir/sofosbuvir based hepatitis C therapy and adalimumab based IBD therapy *Hepatology* 2016; 63(1):474A. PMID: Not assigned. Abstract

M.A. Siddiqui, Internal Medicine, Henry Ford Hospital, Detroit, United States

Purpose: We evaluated the success rate for insurance approval for a single center setting for hepatitis C therapy involving ledipasvir/sofosbuvir and compared it to IBD therapy involving Adalimumab. Methods: Pharmaceutical records were reviewed for all patients prescribed ledipasvir/sofosbuvir and Adalimumab between July 2014 and November 2015. Data was extracted including type of insurance, insurance approval, fibrosis staging based on fibroscan for the patients who were prescribed ledipasvir/sofosbuvir and data for type of IBD, severity of anemia, location, extraintestinal manifestations and perianal complications was collected for the patients who were prescribed Adalimumab. Results: 783 patients were prescribed therapy with ledipasvir/sofosbuvir based therapy and the overall approval rate was 77.8%. In comparison ammong the 55 patients who were prescribed Adalimumab 52 (94.5%) were approved, 2 patients were denied and 1 was still pending approval. Among the patients who were prescribed ledipasvir/ sofosbuvir by insurance companies 296 patients (37.8%) had Medicare, 424 (54.1%) private insurance and (8.2%) had Medicaid. The approval rates were 93% for Medicare patients, 79% for private insurances and 32% for Medicaid patients. Amongst private insurances, Private A had approval rate of 87%, Private B had approval rate of 73% and other private insurances had approval of 71%. In the Adalimumab group, 7.3% patients had Medicare and Medicaid each, 14.6% patients had Private A, 69.1% had Private B and 1.8% had other private insurance. All the patients who had Medicaid or Medicare were approved. Of the 2 patients who were denied one had Private B, Crohn's disease as the diagnoses and absence of anemia or extraintestinal manifestations. Whereas the second patient had insurance other than Private A or B, Ulcerative colitis as the diagnoses, presence of moderate anemia and no extra-intestinal manifestations. Conclusion: We evaluated insurance approval rates of ledipasvir/ sofosbuvir based hepatitis C therapy and Adalimumab based IBD therapy. The over-all approval rate of therapy based on ledipasvir/sofosbuvir was 77.8% and Medicaid patients had a very low approval rate of 32%. The overall approval rate for Adalimumab based therapy was 94.5% and all the Medicare and Medicaid patients were approved. The only patients who were denied had private insurance. (Table Presented).

Gastroenterology
Siddiqui MA, Iraqi H, **Aggarwal R**, **Varma A**, **El Atrache M**, and **Jafri SM**. Insurance approval rates for medicaid patients: A comparison between ledipasvir/sofosbuvir based hepatitis C therapy and adalimumab based IBD therapy *Am J Gastroenterol* 2016; 111:S365. PMID: Not assigned. Abstract

M.A. Siddiqui, Henry Ford Hospital, Detroit, United States

Introduction: Numerous challenges to diagnosing, establishing care, and receiving ledipasvir/sofosbuvir based Hepatitis C therapy exist. There are limited data on insurance authorization for these medications. This generally appears to e a major barrier to receiving therapy. We evaluated the success rate for insurance approval for a single center setting for hepatitis C therapy involving ledipasvir/sofosbuvir and compared it to Inflammatory Bowel Disease (IBD) therapy involving Adalimumab. Methods: Pharmaceutical records were reviewed for all patients prescribed ledipasvir/sofosbuvir and Adalimumab between July 2014 and November 2015. Data was extracted including type of insurance, insurance approval, fibrosis staging based on fibroscan for the patients who were prescribed ledipasvir/sofosbuvir and data for type of IBD, severity of anemia, location, extraintestinal manifestations and perianal complications was collected for the patients who were prescribed Adalimumab. Two-Sample T-Test, Cochran-Armitage Trend Test and Chi-Square Test were run on the data extracted. Results: 783 patients were prescribed therapy with ledipasvir/sofosbuvir based therapy and the over-all approval rate was 77.8%. In comparison ammong the 55 patients who were prescribed Adalimumab 52 (94.5%) were approved, 2 patients were denied and 1 was still pending approval. For the patients who were prescribed ledipasvir/sofosbuvir and had Medicaid only 32% were approved (p value 0.001) wheres all the pateints who were prescibed Adalimumab and had Medicaid were approved. The approval rates for Medicaid patients was poor across all fibrosis stages. Conclusion: Our results suggest that having Medicaid can be a real barrier to receiving ledipasvir/ sofosbuvir for Hepatitis C treatment as compared to other expensive drugs like Adalimumab for IBD treatment. Patients with Medicare and Private insurance had much better approval rates. The stage of fibrosis did significantly impact approval rate. Patients having stage 1 fibrosis had

approval rate of 74.2% while patients having stage 4 fibrosis had approval rate 88.9% (p-value 0.009). For Medicaid patients the approval rate was poor across all fibrosis stages. Even patients with stage 4 fibrosis had an approval rate of only 50%.

Gastroenterology

Siddiqui MA, Tang J, Khan S, **El Atrache M**, **Varma A**, **Aggarwal R**, and **Jafri SM**. A case of necrotising pancreatitis following ampullary biopsy *Am J Gastroenterol* 2016; 111:S549-S550. PMID: Not assigned. Abstract

M.A. Siddiqui, Henry Ford Hospital, Detroit, United States

Acute pancreatitis is a rare, but potential complication of ampullary biopsy. Most patients will recover without major complications. However, 20% of patients will develop a moderate or severe acute pancreatitis with local or systemic complications or organ failure. The patients who develop organ failure or infected necrosis face an increased mortality rate of 30%. To the best of authors knowledge this case represents one of four published articles that reports acute pancreatitis as a complication of ampullary manipulation. A 72 year old male with a past medical history of recurrent ampullary adenomas presented for a routine EGD and colonoscopy. Patient was discharged home and the ampullary biopsies showed no abnormalities. Later that day, the patient presented to the emergency department with acute epigastric pain that radiated to his back with nausea and vomiting. He was hemodynamically stable and afebrile on arrival. He was tender to palpation but exhibited no signs of peritonitis. Initial lab tests showed lipase >2250. Liver function tests, leukocyte count and lipid panel were all within normal limits. He does not drink, take any medications, or have any other risk factor that could potentially be a cause of his pancreatitis. Thus, he was diagnosed with acute pancreatitis secondary to EGD with ampullary biopsy. The patient's epigastric pain did not improve the first 4 days after conservative management with aggressive intravenous fluids and pain control. He started spiking fevers with no known source. A CT abdomen was done and it showed that the patient had developed necrotizing pancreatitis and was started on cefepime and metronidazole. His course was further complicated by non-cardiogenic pulmonary edema which improved after fluids were stopped and a trial of furosemide. He clinically improved and was discharged on day 8 to resume Ciprofloxacin and Metronidazole for a total 21 days. This case reflects one of four case reports of patients developing acute pancreatitis following ampullary biopsy, three of which also developed pancreatic necrosis. Physicians should be aware of acute pancreatitis as a rare but potential complication of endoscopy with ampullary biopsy. If patients do develop acute pancreatitis, it is essential to manage them with adequate fluid resuscitation and to remain vigilant for signs of necrotizing pancreatitis which has a very high mortality rate.

Gastroenterology

Souther B, **Arnautovic J**, and **Singh G**. Ischemic colitis complicated by consumptive coagulopathy *Am J Gastroenterol* 2016; 111:S1306-S1307. PMID: Not assigned. Abstract

B. Souther, Henry Ford Health System, Warren, United States

Colonic ischemia-induced reperfusion injury can lead to multisystem organ failure, regardless of ischemic colitis etiology. However, it rarely leads to consumptive coagulopathy. A review of the current literature shows that there have been limited reported cases of colonic ischemia-induced consumptive coagulopathy. Known etiologies of disseminated intravascular coagulopathy (DIC) include sepsis, malignancy, trauma, and intravascular hemolysis. Ischemic colitis is not a known cause of disseminated intravascular coagulopathy; however, we can relate it to the mechanism of sepsis-induced disseminated intravascular coagulopathy as sepsis is frequently complicated by disseminated intravascular coagulopathy. Disseminating intravascular coagulopathy is the activation of intravascular coagulation culminating in intravascular fibrin formation and deposition into the microvasculature. Secondary fibrinolysis accompanies coagulation activation. Intravascular deposition of fibrin in sepsis leads to a diffuse obstruction of the microvascular bed resulting in progressive organ dysfunction, such as in acute respiratory distress syndrome, acute kidney injury, hypotension, and shock liver. Both the coagulation activation and the consumption of coagulation inhibitors leading to anticoagulation pathways are activated in sepsis, leading to consumptive coagulopathy. Consumptive coagulopathy was an unexpected response to ischemic colitis. We present a case of a 71 year old Hispanic female with past medical history significant for hypertension presented to our facility with sudden onset diffuse abdominal pain and bright red blood per rectum. Work up revealed hematologic profile significant for DIC in addition to acute kidney injury and ischemic hepatitis, negative for schistocytes on peripheral blood smear. Colonoscopy revealed severe ischemic colitis with submucosal hemorrhage and necrosis involving descending colon. Biopsy from colonoscopy was consistent with observation, revealing acute colitis with focal ischemic changes, granulation tissue, and acute inflammatory exudate of descending colon. We believe that the intense inflammatory reaction of ischemic colitis led to this consumptive coagulopathy. While the known etiologies of disseminated intravascular coagulopathy are numerous, ischemic colitis is rarely presented as one. (Table Presented).

Gastroenterology
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, and Holmberg SD. Uptake of and factors associated with direct-acting antiviral therapy among patients infected with hepatitis C virus in the chronic hepatitis cohort study, 2014-2015 *Hepatology* 2016; 63(1):10A-11A. PMID: Not assigned. Abstract

P.R. Spradling, Division of Viral Hepatitis, CDC, Atlanta, United States

Background: Limited information is available describing the uptake of direct acting antiviral (DAA) therapy for hepatitis C virus (HCV) infection among patients in general US healthcare settings. Methods: We analyzed data collected from HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS), an observational cohort study involving patients from healthcare organizations in Michigan, Pennsylvania, Oregon, and Hawaii, limiting analysis to patients with a clinical encounter during the previous two years. Uptake was defined as the proportion of patients infected with HCV as of December 31, 2013 who were prescribed a DAA regimen (with or without interferon) during 2014 and started the regimen by August 31, 2015. Using multivariable analysis and controlling for relevant variables, we examined demographic and clinical characteristics associated with receipt of DAAs. Results: The cohort was comprised of 10,293 HCV-infected patients as of December 31, 2013, of whom 544 (5.3%) started a DAA regimen by August 31, 2015. Factors independently associated with receipt of DAAs included higher annual income (adjusted Odds Ratios [aOR] 2.4 and 1.7 for income >$50K and $30K-$50K, respectively, vs. <$30K), higher FIB4 score (aORs 2.1, 2.0, and 1.5 for FIB4 >5.88, 3.25-5.88, 2.0-<3.25, respectively, vs. <2.0), genotype 2 infection (aOR 2.2, vs. genotype 1), higher Charlson comorbidity score (aORs 1.3 and 1.4 for scores ≥2 and 1, respectively, vs. score of 0), pre-2014 treatment failure (aOR 1.9, vs. treatment-naive), and HIV coin fection (aOR 1.9, vs. HCV monoinfection). Factors associated with a reduced likelihood of DAA receipt included non-Hispanic Black race/ethnicity (aOR 0.7, vs. non-Hispanic Whites), having Medicaid coverage (aOR 0.5, vs. private insurance), and receipt of care at one of the study sites (aOR 0.3, vs. a tertiary hepatology referral site). Sex, age, and duration of follow- up were not associated with receipt of DAAs. Conclusions: Among patients in these general US healthcare settings, uptake of DAA therapy was low from January 2014-August 2015, and especially so among minority and Medicaid patients. Targeted efforts to improve access to DAAs for these patients are essential to reduce morbidity and mortality from HCV infection.

Gastroenterology
Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, and Holmberg SD. Preliminary clinical outcome data among patients with hepatitis C virus infection receiving direct-acting antiviral therapy in the Chronic Hepatitis Cohort Study, 2014-2015 *Hepatology* 2016; 63(1):487A-488A. PMID: Not assigned. Abstract

P.R. Spradling, Division of Viral Hepatitis, CDC, Atlanta, United States

Background: Data describing clinical outcomes of direct-acting antiviral (DAA) therapy among patients infected with hepatitis C virus (HCV) in general healthcare settings are limited. We examined DAA-associated outcomes among HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS), an observational study conducted at 4 US healthcare organizations. Methods: Patients who began a DAA regimen from January 2014-August 2015 were included in the analysis. We examined frequency of treatment completion and of sustained viral response (SVR) 12 weeks post-treatment vs. no SVR by sociodemographic, clinical, and treatment-related factors, and conducted multivariable analysis to identify factors independently associated with SVR. Results: Of 613 patients who began an initial DAA regimen during the study period, 212 (48%) were treatment experienced, 210 (54%) had cirrhosis, 81 (18%) were of black race, and 24 (5%) were HIV-coinfected: 280 (46%) had HCV genotype 1a (G1a); 136 (22%) had G1b; 107 (17%) had G2; 68 (11%) had G3; 5 (1%) had G4-6; and 17 (3%) had mixed genotype infection. Overall, 401 (65%) patients received a sofosbuvir (SOF) regimen without ledipasvir (LDV) (i.e., SOF ± simeprevir or daclatasvir ± ribavirin [RBV]) and 211 (34%) received SOF with LDV ± RBV. No patients received an ombitasvir-containing regimen. Of 545 (89% of 613) patients with available SVR data, 463 (85%) achieved SVR. Among patients with G1a, frequencies of SVR ranged from 77% (SOF without LDV and no RBV) to 96% (SOF with LDV ± RBV); among those with G1b, 70% (SOF regimen without LDV + RBV) to 98% (SOF with LDV ± RBV). The frequency of SVR was 83%, 80% and 75% among patients with G2, G3, and G4-6 infection, respectively. In multivariable analysis controlling for all variables, the sole factor independently associated with SVR was receipt of SOF with LDV ± RBV (aOR 6.1 vs. SOF regimen without LDV and no RBV). Neither age, sex, race/ethnicity, previous treatment status, presence of cirrhosis, genotype, comorbidity score, body mass index, or HIV coinfection were associated with SVR. Of the 613 patients who initiated treatment, 68 (11%) either had completed treatment but did not yet have SVR data available (n=32), were still receiving treatment at the close of the study period (n=22), or stopped treatment early (n=14). Conclusions: Among patients who received DAAs in these general healthcare settings, half of whom had cirrhosis and previous treatment, the frequency of treatment completion and SVR was high. Receipt of a regimen other than SOF with LDV was associated with a lower likelihood of achieving SVR.

Gastroenterology
Teshale EH, Zhong Y, Moorman AC, Spradling PR, Holmberg SD, **Rupp LB**, **Lu M**, **Gordon SC**, Boscarino JA, Daida Y, and Schmidt MA. Alcohol use disorder among chronic hepatitis C patients: Prevalence and treatment outcome, CHeCS, 2006-2013 *Hepatology* 2016; 63(1):873A-874A. PMID: Not assigned. Abstract

E.H. Teshale, CDC, Atlanta, United States

Background: Alcohol use in patients with chronic hepatitis C (CHC) results in progression of liver disease and represents a barrier to antiviral therapy. We sought to determine the prevalence of alcohol abuse and alcohol-related liver disease among CHC patients to assess their access to HCV treatment. Methods: We used CHeCS data collected from CHC patients seen in four large U.S. healthcare systems from 2006-2013. Among patients with documented ICD 9 codes indicative of any alcohol use disorder defined as alcohol abuse/dependence and alcohol-related liver disease, we determined the percentage of patients with any alcohol disorder, with alcohol abuse/dependence, and with alcohol-related liver disease who received HCV treatment. We used multivariable analysis to identify factors associated with HCV treatment by alcohol status. Results: Of the 11,636 CHC patients, 3,553 (30.5%) had at least one documented ICD-9 code indicative of any alcohol use disorder. Among those with any alcohol use disorder, 70.4% were male, 92.5% were aged >44 years, 58.7% were white, and 19.9% had alcohol-related liver disease. Overall, 40.3% of CHC patients received HCV treatment. Only 30.4% of those with alcohol abuse and 50.4% of those with alcohol-related liver disease received treatment. Sustained virologic response rates were 41.6% overall, 44.7% for those with alcohol abuse, and 28.4% for those with alcohol-related liver disease. In univariate analysis HCV treatment was associated with age, race, household income, ever having biopsy and biopsy stage ($p<0.01$). Controlling for age, gender, race, and household income, persons with alcohol abuse were less likely [adjusted odds ratio (aOR) = 0.54 (0.48-0.61)] and those with alcohol- related liver disease were more likely [aOR =1.38 (1.18- 1.63)] to receive HCV treatment than those with no alcohol use disorder. Conclusion: Approximately one third of CHC patients had a recorded diagnosis, indicative of an alcohol use disorder. Although patients diagnosed with alcohol-related liver disease were more likely to receive HCV treatment than those with an alcohol abuse diagnosis, treatment and the response to treatment for patients with either diagnosis were suboptimal overall. Effective direct acting antiviral treatment with greater tolerability and of shorter duration may improve the likelihood of treatment and treatment outcome among all patients, including those with an alcohol use disorder.

Gastroenterology
Weick A, and **Lee A**. Statin-induced liver injury mimicking autoimmune hepatitis *Am J Gastroenterol* 2016; 111:S864. PMID: Not assigned. Abstract

A. Weick, Henry Ford Hospital, Detroit, United States

Introduction: HMG CoA reductase inhibitors (statins) are known to be a cause of hepatic dysfunction, with an incidence of transaminimitis from 0.5 to 3 percent, usually within the first 3 to 4 months of initiating therapy. Here we present a case of acute statin induced liver injury mimicking autoimmune hepatitis. Case Patient is a 70 year old male who initially presented with fatigue, scleral icterus, and a 50 pound weight loss over 3 months. Four months before, he had been started on atorvastatin 40 mg daily which was held on admission. Initial workup showed AST 113 IU/L, ALT 197 IU/L, alkaline phosphatase 944 IU/L (with elevated GGT), and total bilirubin 7.6 g/dL. His INR was 1.15 and creatinine and blood urea nitrogen were 9.53 mg/dL and 121 mg/dL, respectively (no preceding renal dysfunction). Viral hepatitis serologies were negative, and the patient denied any alcohol or acetaminophen use. An MRCP was negative for any biliary obstruction. Urinalysis showed granular casts consistent with acute tubular necrosis. He also had positive smooth muscle antibody, elevated IgG at 2458 mg/dL, positive ANA with 1:1280 titer in a speckled pattern, and positive C-ANCA with a 1:320 titer. P-ANCA, anti-glomerular basement membrane antibody, liver-kidney microsomal antibody, and anti-mitochondrial antibody were negative. Liver biopsy revealed mild mixed portal inflammation and reactive changes with portal fibrosis consistent with a drug reaction, without evidence of autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, or hypotensive changes. Kidney biopsy showed mild acute tubulointerstitial nephritis. His AST and ALT also normalized within 3 weeks, to 24 and 38 IU/L, respectively. His alkaline phosphatase improved more slowly, down to 476 IU/L within 3 weeks and total bilirubin improved to 1.3 g/dL. His renal function recovered with supportive care, with creatinine of 0.85 mg/dL within 3 weeks. At outpatient follow up 1 month later, the patient had already gained back 10 pounds, with no residual scleral icterus and improved fatigue. Discussion Statin-associated drug induced liver injury triggering autoimmune hepatitis is rare, with only ten such cases encountered in literature review. These reports often note a liver biopsy consistent with autoimmune hepatitis, which we did not observe. Most cases have required treatment with immunosuppressant medications, while our patient has so far recovered just by holding the statin medication.

Gastroenterology
Wyles DL, Wedemeyer H, Reddy KR, Luetkemeyer A, Jacobson IM, Vierling JM, **Gordon SC**, Nahass R, Zeuzem S, Wahl J, Barr E, Nguyen BYT, Robertson M, Wan S, Jumes P, Dutko F, and Martin E. Safety and efficacy of the fixed-dose combination regimen of MK-3682/Grazoprevir/MK-8408 in cirrhotic or non-cirrhotic patients with chronic HCV GT1 infection who previously failed a direct-acting antiviral regimen (C-SURGE) *Hepatology* 2016; 63(1):101A-102A. PMID: Not assigned. Abstract

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Background/Purpose: Patients who have failed an NS5A-containing, direct-acting antiviral (DAA) regimen (ledipasvir/sofosbuvir [LDV/SOF] or elbasvir/grazoprevir [EBR/GZR]) are an unmet medical need because there are limited data (and no approved therapies) to guide physicians in their management. This population may have a higher prevalence of negative predictors such as cirrhosis, prior treatment with interferon, baseline resistance associated variants (RAVs), and further enrichment of baseline and/or emergent RAVs, including dual or multiple RAVs. The aim of this trial is to determine the safety and efficacy of the regimen of MK-3682 (NS5B polymerase inhibitor) / grazoprevir (NS3/4A protease inhibitor) / MK-8408 (NS5A inhibitor) in patients who failed a previous DAA regimen. Methods: This multicenter, open-label trial randomized compensated cirrhotic (platelet cutoff=75,000μL; excluded Child-Pugh B &C) or non-cirrhotic HCV GT1-infected patients who relapsed after a recommended regimen of LDV/ SOF or EBR/GZR to receive a once-daily regimen of MK-3682 (450 mg)/grazoprevir (100 mg)/MK-8408 (60 mg) either 16 weeks + ribavirin (RBV) or 24 weeks without RBV. Patients who failed LDV/SOF were stratified by previous 8 or ≥12 week regimen. Next-generation sequencing (15% sensitivity) was used to test for baseline RAVs. The primary objectives of the trial are to determine the efficacy (the proportion of patients with HCV RNA <15 IU/mL at 12 weeks after the end of study therapy; SVR12), and the safety &tolerability of the regimen. Results: 94 GT1 patients were randomized in this trial (78 [83%] GT1a; 16 [17% GT1b]; 64 [68%] HCV RNA >1 million IU/mL at screening). Patients had failed 12 or 24 weeks of LDV/SOF (59 [63%]), 8 weeks of LDV/SOF (13 [14%]), or 12 weeks of EBR/GZR (22 [23%]). Forty-two patients (45%) had cirrhosis. More than 75% of patients had at least 1 NS5A RAV at baseline. Treatment was generally well tolerated in both arms. Most adverse events were mild or moderate and no patient discontinued due to an adverse event. The table shows on-treatment results for the patients who have reached treatment weeks 4 or 8. The SVR4 results and analysis of predictors of outcomes will be presented at the meeting. Conclusions: Preliminary results show that the regimen of MK-3682/grazoprevir/MK-8408 produced robust on-treatment virologic responses and was well-tolerated in cirrhotic and non-cirrhotic GT1 patients who previously failed a direct-acting antiviral regimen. (Table Presented).

Gastroenterology
Younossi ZM, **Gordon SC**, Dieterich DT, Wong R, **Brown KA**, Kugelmas M, Saab S, and Ahmed A. A Decision analytic markov model to evaluate the health outcomes of sofosbuvir/velpatasvir for patients with chronic hepatitis C virus genotype 1 infection in the US *Hepatology* 2016; 63(1):421A-422A. PMID: Not assigned. Abstract

Z.M. Younossi, Inova Fairfax Hospital, Falls Church, United States

BACKGROUND AND AIM: Sofosbuvir / velpatasvir (SOF/ VEL) is an oral single tablet regimen that has been shown in the clinical trial setting to have excellent efficacy and tolerability in treatment-naïve (TN) and treatment-experienced (TE) patients with chronic hepatitis C virus (HCV) genotype 1 (GT1). A decision-analytic Markov model evaluated the health outcomes of SOF/VEL compared with current treatment options for GT1. METHODS: The analysis modeled two cohorts of 10,000 chronic HCV GT1 patients (non-cirrhotic (NC); cirrhotic (CC)) with an average age of 52 from a US third-party payer perspective over a lifetime horizon. 70% of each cohort was TN. SOF/VEL for 12W was compared with LDV/SOF for 8W, 12W +/- ribavirin (RBV), and 24W, elbasvir/grazoprevir (EBR/GRZ) +/- RBV for 12W or 16W, and no treatment (NT). Sustained virologic response (SVR) rates were extrapolated from Phase III clinical trials and stratified by baseline NS5A resistance associated variant for EBR/GRZ. Transition probabilities and utilities were based on a literature review and consensus by a panel of hepatologists. RESULTS: Initiation of SOF/VEL in GT1 patients resulted in the best health outcomes in terms of the lowest numbers of patients with liver-related complications compared with EBR/GRZ, LDV/SOF, and NT (Table 1). Results were consistent across patient subpopulations, including TN, pegintereron+ribavirin (PR)-TE, PR+protease inhibitor-TE, NC, and CC. CONCLUSIONS: Compared to EBR/GRZ and LDV/ SOF, SOF/VEL demonstrated better overall health outcomes in GT1, with reductions up to 58%, 47% and 54% in cases of decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), and liver transplant (LT), respectively. Our results highlight the longer-term benefits of treating chronic HCV with SOF/VEL versus currently available options. (Table Presented).

Gastroenterology
Younossi ZM, Park H, Dieterich D, Saab S, Ahmed A, and **Gordon SC**. The value of cure associated with treating treatment-naive chronic hepatitis C genotype 1: Are the new all-oral regimens good value to society? *Liver Int* 2016;PMID: 27804195. Full Text

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Henry Ford Hospital, Detroit, MI, USA.

BACKGROUND & AIMS: All-oral regimens are associated with high cure rates in hepatitis C virus-genotype 1 (HCV-GT1) patients. Our aim was to assess the value of cure to the society for treating HCV infection. METHODS: Markov model for HCV-GT1 projected long-term health outcomes, life years, and quality-adjusted life years (QALYs) gained. The model compared second-generation triple (sofosbuvir+pegylated interferon+ribavirin [PR] and simeprevir+PR) and all-oral (ledipasvir/sofosbuvir and ombitasvir+paritaprevir/ritonavir+dasabuvir+/-ribavirin) therapies with no treatment. Sustained virological response rates were based on Phase III RCTs. We assumed that 80% and 95% of HCV-GT1 patients were eligible for second-generation triple and all-oral regimens. Transition probabilities, utility and mortality were based on literature review. The value of cure was calculated by the difference in the savings from the economic gains associated with additional QALYs. RESULTS: Model estimated 1.52 million treatment-naive HCV-GT1 patients in the US. Treating all eligible HCV-GT1 patients with second-generation triple and all-oral therapies resulted in 3.2 million and 4.8 million additional QALYs gained compared to no treatment respectively. Using $50,000 as value of QALY, these regimens lead to savings of $185 billion and $299 billion; costs of these regimens were $109 billion and $128 billion. The value of cure with second-generation triple and all-oral regimens was $55 billion and $111 billion, when we conservatively assumed only drug costs. Cost savings were greater for HCV-GT1 patient cured with cirrhosis compared to patients without cirrhosis. CONCLUSIONS: The recent evolution of regimens for HCV GT1 has increased efficacy and value of cure.

Hypertension and Vascular Research
Karuppagounder V, Arumugam S, Babu SS, **Palaniyandi SS**, Watanabe K, Cooke JP, and Thandavarayan RA. The senescence accelerated mouse prone 8 (SAMP8): A novel murine model for cardiac aging *Ageing Res Rev* 2016;PMID: 27825897. Full Text

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Because cardiovascular disease remains the major cause of mortality and morbidity world-wide, there remains a compelling need for new insights and novel therapeutic avenues. In this regard, the senescence-accelerated mouse prone 8 (SAMP8) line is a particularly good model for studying the effects of aging on cardiovascular health. Accumulating evidence suggests that this model may shed light on age-associated cardiac and vascular dysfunction and disease. These animals manifest evidence of inflammation, oxidative stress and adverse cardiac remodeling that may recapitulate processes involved in human disease. Early alterations in oxidative damage promote endoplasmic reticulum stress to trigger apoptosis and cytokine production in this genetically susceptible mouse strain. Conversely, pharmacological treatments that reduce inflammation and oxidative stress improve cardiac function in these animals. Therefore, the SAMP8 mouse model provides an exciting opportunity to expand our knowledge of aging in cardiovascular disease and the potential identification of novel targets of treatment. Herein, we review the previous studies performed in SAMP8 mice that provide insight into age-related cardiovascular alterations.

Hypertension and Vascular Research
Pan G, Deshpande M, Thandavarayan RA, and **Palaniyandi SS**. ALDH2 Inhibition potentiates high glucose stress-induced injury in cultured cardiomyocytes *J Diabetes Res* 2016; 2016:1390861. PMID: 27882330. Full Text

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Department of Cardiovascular Sciences, Center for Cardiovascular Regeneration, Houston Methodist Research Institute, Houston, TX, USA.
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Aldehyde dehydrogenase (ALDH) gene superfamily consists of 19 isozymes. They are present in various organs and involved in metabolizing aldehydes that are biologically generated. For instance, ALDH2, a cardiac mitochondrial ALDH isozyme, is known to detoxify 4-hydroxy-2-nonenal, a reactive aldehyde produced upon lipid peroxidation in diabetic conditions. We hypothesized that inhibition of ALDH leads to the accumulation of unmetabolized 4HNE and consequently exacerbates injury in cells subjected to high glucose stress. H9C2 cardiomyocyte cell lines were pretreated with 10 muM disulfiram (DSF), an inhibitor of ALDH2 or vehicle (DMSO) for 2 hours, and then subjected to high glucose stress {33 mM D-glucose (HG) or 33 mM D-mannitol as an osmotic control (Ctrl)} for 24 hrs. The decrease in ALDH2 activity with DSF pretreatment was higher in HG group when compared to Ctrl group. Increased 4HNE adduct formation with DSF pretreatment was higher in HG group compared to Ctrl group. Pretreatment with DSF leads to potentiated HG-induced cell death in cultured H9C2 cardiomyocytes by lowering mitochondrial membrane potential. Our results indicate that ALDH2 activity is important in preventing high glucose induced cellular dysfunction.

Hypertension and Vascular Research
Staruschenko A, Ilatovskaya DV, and **Pavlov TS**. High salt diet and caffeine: food for thought *J Thorac Dis* 2016; 8(10):E1410-e1412. PMID: 27867643. Full Text

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Infectious Diseases
Bardossy AC, **Jayaprakash R**, **Alangaden AC**, **Starr P**, **Abreu-Lanfranco O**, **Reyes K**, **Zervos MJ**, and **Alangaden GJ**. Impact and limitations of the 2015 national health and safety network case definition on catheter-associated urinary tract infection rates *Infect Control Hosp Epidemiol* 2016:1-3. PMID: 27881213. Full Text

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Application of the new 2015 NHSN definition of catheter-associated urinary tract infection (CAUTI) in intensive care units reduced CAUTI rates by ~50%, primarily due to exclusion of candiduria. This significant reduction in CAUTI rates resulting from the changes in the definition must be considered when evaluating effectiveness of CAUTI prevention programs. Infect Control Hosp Epidemiol 2016;1-3.

Infectious Diseases
Carreno JJ, Kenney RM, **Divine G**, **Vazquez JA**, and **Davis SL**. Randomized controlled trial to determine the efficacy of early switch from vancomycin to vancomycin alternatives as a strategy to prevent nephrotoxicity in patients with multiple risk factors for adverse renal outcomes (STOP-NT) *Ann Pharmacother* 2016;PMID: 27838680. Full Text

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BACKGROUND: Use of alternative antimicrobials to vancomycin is a potential strategy to reduce acute kidney injury (AKI) in high-risk patients, but current data do not support widespread adoption of this practice. OBJECTIVE: To determine the efficacy of early switch to a nonnephrotoxic alternative for prevention of AKI in high-risk patients who receive vancomycin. METHODS: This was an IRB-approved, prospective randomized controlled trial in a single, tertiary care academic medical center. Patients initially prescribed vancomycin between October 2011 to April 2013 with at least 2 risk factors for AKI were included. Treatment randomization was stratified by indication for therapy. Patients were randomized to continuation of dose-optimized vancomycin or early switch to an alternative antimicrobial agent. The primary end point was nephrotoxicity by consensus guideline definition adjudicated by

blinded review; the secondary end point was AKI network-defined AKI. RESULTS: A total of 103 patients were randomized; 100 were included in the modified intent-to-treat population, 51 in the vancomycin group and 49 in the alternative group. The incidence of nephrotoxicity was 6.1% in the alternative therapy arm and 9.8% in the vancomycin group (P = 0.72). The incidence of AKI was 32.7% in the alternative therapy group and 31.4% in the vancomycin group (P = 0.89). CONCLUSIONS: No significant difference in nephrotoxicity or AKI was detected among patients treated with alternative antimicrobials compared with vancomycin. The use of alternative antimicrobial therapy instead of vancomycin solely for the purpose of preventing AKI in high-risk patients does not appear to be warranted.

Infectious Diseases
Gildeh E, **Abdel-Rahman Z**, **Sengupta R**, and **Johnson L**. A case of false-positive mycobacterium tuberculosis caused by mycobacterium celatum *Case Rep Infect Dis* 2016; 2016:1761923. PMID: 27895946. Full Text

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Mycobacterium celatum is a nontuberculous mycobacterium shown to cause symptoms similar to pulmonary M. tuberculosis. Certain strains have been shown to cross-react with the probes used to detect M. tuberculosis, making this a diagnostic challenge. We present a 56-year-old gentleman who developed signs and symptoms of lung infection with computed tomography scan of the chest showing right lung apex cavitation. Serial sputum samples were positive for acid-fast bacilli and nucleic acid amplification testing identified M. tuberculosis ribosomal RNA, resulting in treatment initiation. Further testing with high performance liquid chromatography showed a pattern consistent with M. celatum. This case illustrates the potential for M. celatum to mimic M. tuberculosis in both its clinical history and laboratory testing due to the identical oligonucleotide sequence contained in both. An increasing number of case reports suggest that early reliable differentiation could reduce unnecessary treatment and public health intervention associated with misdiagnosed tuberculosis.

Infectious Diseases
Kak V. Therapy for cellulitis *Jama* 2016; 316(19):2045-2046. PMID: 27838712. Full Text

Henry Ford Allegiance Health, Jackson, Michigan.

Infectious Diseases
Meighani A, **Ramesh M**, and **Salgia R**. Successful outcomes of fecal microbiota transplantation in patients with chronic liver disease *Hepatology* 2016; 63(1):1016A-1017A. PMID: Not assigned. Abstract

A. Meighani, Internal Medicine, Henry Ford Hospital, Detroit, United States

Background: Fecal Microbiota Transplantation (FMT) has been shown to be a promising treatment option for patients with recurrent and/ or refractory Clostridium Difficile Infection (CDI). Despite increasing research on FMT, little is known about outcomes in patients with liver disease or cirrhosis. We aimed to study the outcomes of FMT in patients with chronic liver disease (CLD) at our tertiary medical center. Methods: A cohort of all patients who had undergone FMT from December 2012 to May 2014 for refractory or recurrent CDI was identified. Patients were followed up for 1 year post-FMT. Response to treatment was defined as resolution of symptoms in 7 days. Severe CDI was defined as a rise in creatinine >1.5 times above baseline, WBC ≥ 15,000 cells/mL, or albumin < 1.5 g/ dl within 2 weeks of symptom onset. Descriptive analysis was performed to determine the outcomes of FMT in patients with CLD as compared to the comparison cohort without liver disease. Results: A total of 201 patients underwent FMT for CDI, from which 14 had a history of chronic liver disease. Nine of these patients had cirrhosis with a mean Child-Turcotte-Pugh (CTP) score of 8. One patient was 5 months post-liver transplant at the time of FMT. Mean age of patients in the liver disease cohort was 62 with 71% being female. Recent antibiotic use was a common risk factor related to CDI development and was found to be significantly different between both groups (17% of CLD patients vs 58% in the general cohort, p= 0.01). Although some patients were immunosuppressed due to history of IBD or liver transplant, there was no significant difference between the two groups and their outcomes in terms of immunosuppression, route of FMT delivery, number of CDI infections within the prior 3 months, recent hospitalization, recent surgeries or Charlson comorbidity index. There was no significant difference in the number of patients with severe grading of CDI among patients with CLD and the general cohort (36% vs 24%, p= 0.34). Four patients with CLD received >1 FMT, of which 2 remained non-responders. Overall, there was no significant difference in FMT response between patients with liver disease and the rest of the cohort (12/14, 87% vs 164/187, 88%, p= 0.68). Both patients who failed FMT in the CLD cohort had decompensated cirrhosis with CTP scores of 9 and 12, respectively. Conclusion: Fecal

microbiota transplantation is a safe and successful treatment option for patients with recurrent and/or refractory CDI who have stable chronic liver disease or compensated cirrhosis. Recent antibiotic use was less commonly a risk factor for CDI in patients with liver disease.

Infectious Diseases
Suleyman G, and **Alangaden GJ**. Nosocomial fungal infections: Epidemiology, infection control, and prevention *Infect Dis Clin North Am* 2016; 30(4):1023-1052. PMID: 27816138. Full Text

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Invasive fungal infections are an important cause of morbidity and mortality in hospitalized patients and in the immunocompromised population. This article reviews the current epidemiology of nosocomial fungal infections in adult patients, with an emphasis on invasive candidiasis and aspergillosis. Recently published recommendations and guidelines for the control and prevention of these nosocomial fungal infections are summarized in this article.

Internal Medicine
Aguin V, **Meighani A**, **Hussain S**, **Atrache ME**, **Elbatta M**, **Bukannan A**, **Jafri SM**, and **Ibrahim M**. Elevated head of the bed, a novel position for performing colonoscopy: Does it improve the quality of the examination? *Am J Gastroenterol* 2016; 111:S141. PMID: Not assigned. Abstract

V. Aguin, Henry Ford Health System, Detroit, United States

Introduction: Colonoscopy is currently considered to be the gold standard for colon cancer screening. Cecal intubation rate, withdrawal time and adenoma detection rate are acknowledged as quality measures for colonoscopy. We feel that terminal ileum intubation rate would add to the diagnostic quality of colonoscopy. Shortening of cecal intubation time and total procedure time would improve the patient comfort and the economics of the procedure. We evaluated the impact of elevating the head of the bed on these quality measures of colonoscopy. Methods: We performed a retrospective electronic medical records (EMR) review of 655 patients who had their screening colonoscopy at a teaching tertiary care hospital. Descriptive analyses and group comparisons were performed between two groups. One group (N = 323) had their colonoscopy performed in a flat left lateral position and the second group (N= 332) had their colonoscopy with the head of the bed elevated 30 degrees. We collected data on their baseline characteristics, cecal intubation time, withdrawal time, total procedure time, terminal ilium intubation, and polyp detection rate. Differences between groups for time variables were tested via independent samples t-tests, while associations between categorical variables and head position were tested with chi-square tests. Results: Elevated position increased the terminal ilium intubation rate to 78.71 % compared to 69.95 % in the standard flat position (p-0.007). Cecal intubation time (mean of 6.35 min), withdrawal time (mean of 10.63 min) and total procedure time (mean of 16.85 min) in the tilted position, were shorter than in the flat position mean of (6.49 min, 10.80 min, and 17.20 min, respectively) (p-0.644, 0.687, 0.499). The polyp detection rate was (53.27%) for the elevated position, which is minimally higher than that for flat position (53.16%). Conclusion: Patients with tilted head of the bed had statistically significant higher rate of terminal ilium intubation, compared to those with a standard flat position. There was a shortening of cecal Intubation time and total procedure time in the tilted position, but it was not statistically significant. In the elevated head group the quality of the examination was not compromised by the faster procedure as indicated by the slightly higher polyp detection rate. A larger number of procedures need to be evaluated in the future to futher assess the positive effects of elevation of the head of the bed on all the quality measures of colonoscopy.

Internal Medicine
Bourgi K, **Brar I**, and **Baker-Genaw K**. Hepatitis C screening and linkage to care at a comprehensive health system *Topics in Antiviral Medicine* 2016; 24(E-1):209. PMID: Not assigned. Abstract

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Background: The Centers for Disease Control and Prevention (CDC) and the United States Preventive Services Task Force (USPTF) recommend screening for Hepatitis C (HCV) among patients born between 1945 and 1965. With the advent of novel highly effective therapies, we evaluated the current HCV screening rates along with linkage to care for patients with active disease. Methods: We used the Henry Ford Health System records to create a retrospective

cohort of patients born between 1945 - 1965 seen at 21 internal medicine clinics between July 2014 and June 2015. Patients previously screened for HCV and those with established disease were excluded. We studied patient socio-demographic and medical conditions along with provider-specific factors associated with likelihood of screening. Patients who tested positive were reviewed to assess appropriate linkage to care and treatment. Results: 47,304 patients were included in our study cohort and 40,561 patients met inclusion criteria. A total of 8,657 (21.3%) were screened. Screening rates were found to be higher among men ($p < 0.001$) and African Americans ($p <0.001$). The rates were lower in patients with multiple comorbidities ($p <0.001$) and fewer clinic visits ($p <0.001$). Practice setting influenced screening rates as patients seen in residency teaching clinics were more likely to be screened ($p <0.001$). Patient electronic health engagement was associated with higher screening rates ($p <0.001$). Among patients who were screened, 117 (1.4 %) patients tested positive. After excluding patients without active viremia, 78% of patients were referred to a Hepatitis C specialist and 50% were successfully evaluated. On follow-up, 27% of HCV positive patients received treatment with Direct Acting Anti-virals. Medicaid patients were less likely to be treated ($p <0.05$) along with a trend towards a decrease in likelihood of treatment among patients with lower income. Electronic health engagement was again a significant factor that increased the odds of treatment ($p <0.05$). Conclusions: HCV screening rates are suboptimal with a significant influence of sociodemographic and provider-specific factors. Furthermore, patients who tested positive had inadequate linkage to care with a major disadvantage for Medicaid and low income patients. This accentuates the need for a more robust and equitable care delivery system. The study also highlights a promising role for patient's engagement in electronic health portals through active linkage at multiple phases of the care cascade. (Table Presented).

Internal Medicine

Brown-Deacon C, Brown T, Creech C, McFarland M, **Nair A**, and Whitlow K. Can follow-up phone calls improve patients self-monitoring of blood glucose? *J Clin Nurs* 2016;PMID: 27862497. Full Text

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AIMS AND OBJECTIVES: To evaluate the effectiveness of follow-up phone calls in improving frequency of glucose monitoring over a three month period in two groups of patients with type 2 diabetes with the goal to lower haemoglobin A1C. BACKGROUND: Telephone intervention has been successfully used in improving adherence to diabetes self-management and other chronic disease conditions. DESIGN: A quality improvement study. METHODS: Forty one Type 2 diabetic patients with HA1C >/=7.5% were included in the study. The patients were assigned to two groups. The first group of patients received standard diabetic care (Group 1) and the second group of patients (Group 2) received standard diabetic care plus follow-up phone calls within two weeks after a monthly clinic visit over a three month period. A haemoglobin A1C if indicated was done at the initial study visit. RESULTS: There were no statistically significant differences in the baseline haemoglobin A1C between the two groups or the three month haemoglobin A1C of the two groups. There were no statistically significant differences in mean haemoglobin A1C change between Group 1 and Group 2. The analysis revealed that there were no statistically significant differences between groups in the number of patients who kept logs of their blood glucose readings throughout the study. CONCLUSION: The intervention using telephone follow-up calls did not show a statistically significant improvement in overall HA1C, but there was a clinically significant change in HA1C in the group of patients that received follow-up phone calls. RELEVANCE TO CLINICAL PRACTICE: The clinical significance of the change in A1C in the follow-up phone call group (Group 2) supports that frequent contact by telephone may likely improve adherence to diabetes self-management.

Internal Medicine

Gildeh E, **Abdel-Rahman Z**, **Sengupta R**, and **Johnson L**. A case of false-positive mycobacterium tuberculosis caused by mycobacterium celatum *Case Rep Infect Dis* 2016; 2016:1761923. PMID: 27895946. Full Text

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Mycobacterium celatum is a nontuberculous mycobacterium shown to cause symptoms similar to pulmonary M. tuberculosis. Certain strains have been shown to cross-react with the probes used to detect M. tuberculosis, making this a diagnostic challenge. We present a 56-year-old gentleman who developed signs and symptoms of lung infection with computed tomography scan of the chest showing right lung apex cavitation. Serial sputum samples were positive for acid-fast bacilli and nucleic acid amplification testing identified M. tuberculosis ribosomal RNA, resulting in treatment initiation. Further testing with high performance liquid chromatography showed a pattern consistent with M. celatum. This case illustrates the potential for M. celatum to mimic M. tuberculosis in both its clinical history and laboratory testing due to the identical oligonucleotide sequence contained in both. An increasing

number of case reports suggest that early reliable differentiation could reduce unnecessary treatment and public health intervention associated with misdiagnosed tuberculosis.

Internal Medicine
Hale ZD, Kong X, Haymart B, Gu X, Kline-Rogers E, Almany S, Kozlowski J, **Krol GD**, **Kaatz S**, Froehlich JB, and Barnes GD. Prescribing trends of atrial fibrillation patients who switched from warfarin to a direct oral anticoagulant *J Thromb Thrombolysis* 2016;PMID: 27837309. Full Text

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Direct oral anticoagulant (DOAC) agents offer several lifestyle and therapeutic advantages for patients relative to warfarin in the treatment of atrial fibrillation (AF). These alternative agents are increasingly used in the treatment of AF, however the adoption practices, patient profiles, and reasons for switching to a DOAC from warfarin have not been well studied. Through the Michigan Anticoagulation Quality Improvement Initiative, abstracted data from 3873 AF patients, enrolled between 2010 and 2015, were collected on demographics and comorbid conditions, stroke and bleeding risk scores, and reasons for anticoagulant switching. Over the study period, patients who switched from warfarin to a DOAC had similar baseline characteristics, risk scores, and insurance status but differed in baseline CrCl. The most common reasons for switching were patient related ease of use concerns (37.5%) as opposed to clinical reasons (16.5% of patients). Only 13% of patients that switched to a DOAC switched back to warfarin by the end of the study period.

Internal Medicine
Henein F, **Prabhakar D**, **Peterson EL**, **Williams LK**, and **Ahmedani BK**. A prospective study of antidepressant adherence and suicidal ideation among adults *Prim Care Companion CNS Disord* 2016; 18(6)PMID: 27907275. Article Request Form

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Internal Medicine
Isaacs SR, **Wang J**, Kim KW, **Yin C**, **Zhou L**, **Mi QS**, and Craig ME. MicroRNAs in type 1 diabetes: Complex interregulation of the immune system, beta cell function and viral infections *Curr Diab Rep* 2016; 16(12):133. PMID: 27844276. Full Text

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Since the discovery of the first mammalian microRNA (miRNA) more than two decades ago, a plethora of miRNAs has been identified in humans, now amounting to more than 2500. Essential for post-transcriptional regulation of gene networks integral for developmental pathways and immune response, it is not surprising that dysregulation of miRNAs is often associated with the aetiology of complex diseases including cancer, diabetes and autoimmune disorders. Despite massive expansion of small RNA studies and extensive investigation in diverse disease contexts, the role of miRNAs in type 1 diabetes has only recently been explored. Key studies using human islets have recently implicated virus-induced miRNA dysregulation as a pivotal mechanism of beta cell destruction, while the interplay between miRNAs, the immune system and beta cell survival has been illustrated in studies using animal and cellular models of disease. The role of specific miRNAs as major players in immune system homeostasis highlights their exciting potential as therapeutics and prognostic biomarkers of type 1 diabetes.

Internal Medicine

Lenhart A, **Fernandez-Castillo J**, **Mullins K**, and **Salgia R**. A rare case of gastric variceal hemorrhage secondary to infiltrative b-cell lymphoma *Case Rep Gastroenterol* 2016; 10(3):518-524. PMID: 27843428. Full Text

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Portal hypertension commonly arises in the setting of advanced liver cirrhosis and is the consequence of increased resistance within the portal vasculature. Less commonly, left-sided noncirrhotic portal hypertension can develop in a patient secondary to isolated obstruction of the splenic vein. We present a rare case of left-sided portal hypertension and isolated gastric varices in a patient with large B-cell lymphoma, who was treated with splenic artery embolization. The patient is a 73-year-old male with no previous history of liver disease, who presented with coffee ground emesis and melena. On admission to hospital, he was found to have a hemoglobin level of 3.4 g/l. Emergent esophagogastroduodenoscopy showed isolated bleeding gastric varices (IGV1 by Sarin classification) in the fundus and cardia with subsequent argon plasma coagulation injection. He was transferred to our tertiary center where work-up revealed normal liver function tests, and abdominal ultrasound showed patent hepatic/portal vasculature without cirrhosis. MRI demonstrated a large heterogeneously enhancing mass in the pancreatic tail, with invasion into the spleen and associated splenic vein thrombosis. Surgery consultation was obtained, but urgent splenectomy was not recommended. The patient instead underwent splenic artery embolization to prevent future bleeding from his known gastric varices. Pathology from a CT-guided biopsy was consistent with diffuse large B-cell lymphoma. PET imaging showed uptake in the splenic hilum/pancreatic tail region with no additional metastatic involvement. He was evaluated by the Hematology Department to initiate R-CHOP chemotherapy. During his outpatient follow-up, he reported no further episodes of melena or hematemesis. To the best of our knowledge, there have only been two published case reports of large B-cell lymphoma causing upper gastrointestinal bleeding from isolated gastric varices. These cases were treated with splenectomy or chemotherapy alone. Thus far, splenectomy has been the standard treatment approach for splenic vein thrombosis with clinical complication, such as gastric variceal bleeding. We present a case of successful treatment of bleeding isolated gastric varices using a less invasive and less morbid approach through splenic artery embolization. This case highlights the need for an increased awareness of the diverse etiologies of left-sided portal hypertension and isolated gastric varices, as well as the consideration of minimally invasive management strategies.

Internal Medicine

Lenhart A, **Hassan M**, **Meighani A**, **Sadiq O**, and **Siddiqui Y**. A perplexing case of abdominal pain that led to the diagnosis of zollinger-ellison syndrome *Am J Gastroenterol* 2016; 111:S1056. PMID: Not assigned. Abstract

A. Lenhart, Henry Ford Hospital, Detroit, United States

Zollinger-Ellison Syndrome (ZES) is a rare clinical disorder, characterized by hypersecretion of gastric acid and multiple ulcers distal to the duodenal bulb. This occurs via the release of gastrin by neuroendocrine tumors known as gastrinomas. Patients with ZES present with nonspecific GI symptoms, which often leads to a delay in diagnosis. We present a case that highlights the importance of increased awareness of ZES in patients with chronic GI complaints. The patient is a 55 year-old female with a history of chronic pancreatitis, who had been following in the GI clinic for several years, secondary to abdominal pain, nausea, and diarrhea. However, despite extensive testing, an etiology of her symptoms had not been determined. She initially underwent esophagogastroduodenoscopy (EGD) and endoscopic ultrasound (EUS), which only showed gastropathy and chronic pancreatitis. Magnetic resonance cholangiopancreatography was unremarkable. She underwent cholecystectomy, but continued to have symptoms, which prompted a repeat EGD. This showed a deep ulceration at the gastro-esophageal junction (LA Grade D), a 2 cm deeply cratered ulcer in the second portion of the duodenum, and a stricture in the third portion of the duodenum (Figure 1). Biopsies showed gastritis and duodenitis without evidence of malignancy. These findings were suspicious

for ZES, and work up was initiated. Serum gastrin level was elevated at 1639 pg/mL, but repeat EUS and CT abdomen/pelvis did not reveal any pancreatic or duodenal masses. Somatostain receptor scintigraphy (SRS) was obtained, which showed two small lesions in the gastrinoma triangle (Figure 2). She subsequently underwent a Whipple pancreaticoduodenectomy. Pathology was positive for four microscopic foci (largest 0.1 cm) of a well-differentiated neuroendocrine tumor with evidence of metastasis to two peri-pancreatic nodes. She reported improvement in her symptoms after surgery. This case highlights the need for increased awareness of ZES in patients with unexplained GI complaints. The time to diagnosis in this patient was over seven years, which may have been reduced if ZES was considered earlier. This case also emphasizes the use of multiple modalities in the diagnosis of ZES. SRS, which ultimately detected the gastrinoma in this patient, has a higher sensitivity than CT/MRI. EUS also has a high sensitivity; however, a pancreatic mass was not identified with EUS in our patient, possibly secondary to the small size of the tumor. (Figure Presented).

Internal Medicine

Liu Y, **Gao X**, **Deeb D**, **Zhang Y**, **Shaw J**, **Valeriote FA**, and **Gautam SC**. Mycotoxin verrucarin A inhibits proliferation and induces apoptosis in prostate cancer cells by inhibiting prosurvival Akt/NF-kB/mTOR signaling *J Exp Ther Oncol* 2016; 11(4):251-260. PMID: 27849335. Article Request Form

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Trichothecenes are powerful mycotoxins that inhibit protein synthesis and induce ribotoxic stress response in mammalian cells. Verrucarin A (VC-A) is a Type D macrocyclic mycotoxin which inhibits cell proliferation and induces apoptosis in cancer cells. However, the antitumor activity of VC-A for prostate cancer cells has not been investigated. The objective of the present study was to determine the anticancer activity and its mechanism of action in hormone-responsive (LNCaP) and hormone-refractory (PC-3) carcinoma of the prostate (CaP) cell lines. VC-A strongly inhibited the proliferation and induced cell cycle arrest in G2/M phase associated with the inhibition of cell cycle regulatory proteins cyclin D, cyclin E, cyclin-dependent kinases (cdks) cdk2, cdk4, cdk6 and cdk inhibitors WAF1/21 and KIP1/27. VC-A also induced apoptosis in CaP cells as characterized by the cleavage of poly (ADP-ribose) polymerase (PARP-1), procaspases-3, -8 and -9 and the inhibition of Bcl-2 family proteins that regulate apoptosis (Bcl-2, Bcl-xL, Bax, Bak and Bad). In addition, VC-A also down-regulated the expression of prosurvival phospho-AKT (p-AKT), nuclear factor kappa B (NF-kB) (p65) and phospho-mammalian target of rapamycin (p-mTOR) signaling proteins. Taken together, these results demonstrated strong antiproliferative and apoptosis-inducing activity of verrucarin A against CaP cells through cell cycle arrest and inhibition of the prosurvival (antiapoptotic) AKT/NF-kB/mTOR signaling pathway.

Internal Medicine

Meighani A, **Hassan M**, **Lenhart A**, and **Gordon S**. Aortitis in a patient with chronic hepatitis C virus infection *Am J Gastroenterol* 2016; 111:S870-S871. PMID: Not assigned. Abstract

A. Meighani, Henry Ford Hospital, Detroit, United States

Chronic hepatitis C virus (HCV) infection is a recognized cause of cryoglobulinemic vasculitis. It is an immune-complex mediated systemic inflammatory syndrome that generally involves small-to-medium sized vessels. Aortitis and other large vessel vasculitides secondary to cryoglobulinemia are very rare and are seldom reported. We report a case of a 70-year old Caucasian male with a past medical history of gout and untreated non-cirrhotic chronic HCV, genotype 1a, who presented with a one-week history of moderately severe, right-sided abdominal pain. He also reported a two-week history of a non-blanching, erythematous, maculo-papular rash on his trunk and back, which was partially relieved by a corticosteroid cream. His work up in the Emergency Department included a CBC that showed leukocytosis of 14 K/uL and a computed tomography (CT) scan of his abdomen with contrast, which showed inflammatory changes near the bifurcation of the aorta. This prompted a CT angiography (CTA) that showed diffuse wall thickening of the distal abdominal aorta and common iliac vessels without evidence of contrast extravasation (Figures 1-2), findings that were suggestive of a focal, large vessel vasculitis. Laboratory studies showed C-reactive protein and erythrocyte sedimentation rate elevated to 8.7 mg/dL and 34 mm/hr, respectively. Rapid plasma reagin test for syphilis was negative. The HCV RNA was 183, 424 IU. Serum for cryoglobulins was positive. The decision was subsequently made to initiate simultaneous treatment with ledipasvir/sofosbuvir as well as oral prednisone of 20 mg daily which was tapered off over 3 months. He completed a total of 12 weeks of therapy and ultimately achieved a sustained virologic response. A follow up magnetic resonance angiography (MRA) was performed four months after his initial presentation, and showed resolution of the previously noted distal abdominal aorta, bilateral common iliac arteries, and proximal bilateral external iliac artery wall thickening (Figure. 3). His CRP and ESR also improved within a month of starting treatment. This case highlights a previously unreported example of large vessel cryoglobulinemic

vasculitis involving the distal aorta, presumably mediated by HCV infection. The rapid improvement following initiation of sofosbuvir/ledipasvir emphasizes the need to search for viral etiology in similar cases and to promptly begin potentially lifesaving therapy. (Figure presented).

Internal Medicine
Meighani A, **Ramesh M**, and **Salgia R**. Successful outcomes of fecal microbiota transplantation in patients with chronic liver disease *Hepatology* 2016; 63(1):1016A-1017A. PMID: Not assigned. Abstract

A. Meighani, Internal Medicine, Henry Ford Hospital, Detroit, United States

Background: Fecal Microbiota Transplantation (FMT) has been shown to be a promising treatment option for patients with recurrent and/ or refractory Clostridium Difficile Infection (CDI). Despite increasing research on FMT, little is known about outcomes in patients with liver disease or cirrhosis. We aimed to study the outcomes of FMT in patients with chronic liver disease (CLD) at our tertiary medical center. Methods: A cohort of all patients who had undergone FMT from December 2012 to May 2014 for refractory or recurrent CDI was identified. Patients were followed up for 1 year post-FMT. Response to treatment was defined as resolution of symptoms in 7 days. Severe CDI was defined as a rise in creatinine >1.5 times above baseline, WBC ≥ 15,000 cells/mL, or albumin < 1.5 g/ dl within 2 weeks of symptom onset. Descriptive analysis was performed to determine the outcomes of FMT in patients with CLD as compared to the comparison cohort without liver disease. Results: A total of 201 patients underwent FMT for CDI, from which 14 had a history of chronic liver disease. Nine of these patients had cirrhosis with a mean Child-Turcotte-Pugh (CTP) score of 8. One patient was 5 months post-liver transplant at the time of FMT. Mean age of patients in the liver disease cohort was 62 with 71% being female. Recent antibiotic use was a common risk factor related to CDI development and was found to be significantly different between both groups (17% of CLD patients vs 58% in the general cohort, p= 0.01). Although some patients were immunosuppressed due to history of IBD or liver transplant, there was no significant difference between the two groups and their outcomes in terms of immunosuppression, route of FMT delivery, number of CDI infections within the prior 3 months, recent hospitalization, recent surgeries or Charlson comorbidity index. There was no significant difference in the number of patients with severe grading of CDI among patients with CLD and the general cohort (36% vs 24%, p= 0.34). Four patients with CLD received >1 FMT, of which 2 remained non-responders. Overall, there was no significant difference in FMT response between patients with liver disease and the rest of the cohort (12/14, 87% vs 164/187, 88%, p= 0.68). Both patients who failed FMT in the CLD cohort had decompensated cirrhosis with CTP scores of 9 and 12, respectively. Conclusion: Fecal microbiota transplantation is a safe and successful treatment option for patients with recurrent and/or refractory CDI who have stable chronic liver disease or compensated cirrhosis. Recent antibiotic use was less commonly a risk factor for CDI in patients with liver disease.

Internal Medicine
Murad MH, Guyatt GH, **Domecq JP**, Vernooij RW, Erwin PJ, Meerpohl JJ, Prutsky GJ, Akl EA, Mueller K, Bassler D, Schandelmaier S, Walter SD, Busse JW, Kasenda B, Pagano G, Pardo-Hernandez H, Montori VM, Wang Z, and Briel M. Randomized trials addressing a similar question are commonly published after a trial stopped early for benefit *J Clin Epidemiol* 2016;PMID: 27832953. Full Text

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Basel Institute for Clinical Epidemiology and Biostatistics, University Hospital Basel, Basel, Switzerland; Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON L8S 4L8, Canada.

OBJECTIVE: We explored how investigators of ongoing or planned trials respond to the publication of a trial stopped early for benefit addressing a similar question. STUDY DESIGN AND SETTING: We searched multiple databases from the date of publication of the truncated trial through August, 2015. Independent reviewers selected trials and extracted data. RESULTS: We identified 207 trials truncated for early benefit; of which 102 (49%) were followed by subsequent trials (262 subsequent trials, median 2 per truncated trial, range 1-13). Only 99 (38%) provided a rationale justifying conducting a trial despite prior stopping. The top reasons were to address different population or setting (33%); skepticism of truncated trials findings because of small sample size (12%), inconsistency with other evidence (11%) or increased risk of bias (7%). We did not identify significant associations between subsequent trials and characteristics of truncated ones (risk of bias, precision, funding, or rigor of stopping decision). CONCLUSION: About half of the trials stopped early for benefit were followed by subsequent trials addressing a similar question. This suggests that future trialists may have been skeptic about the decision to stop prior trials. A more rigorous threshold for stopping early for benefit is needed.

Internal Medicine

Prutsky G, **Domecq JP**, Salazar CA, and Accinelli R. Antifibrinolytic therapy to reduce haemoptysis from any cause *Cochrane Database Syst Rev* 2016; 11:Cd008711. PMID: 27806184. Full Text

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BACKGROUND: Haemoptysis is a common pathology around the world, occurring with more frequency in low-income countries. It has different etiologies, many of which have infectious characteristics. Antifibrinolytic agents are commonly used to manage bleeding from different sources, but their usefulness in pulmonology is unclear. OBJECTIVES: To evaluate the effectiveness and safety of antifibrinolytic agents in reducing the volume and duration of haemoptysis in adult and paediatric patients. SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE) in The Cochrane Library, EMBASE and LILACS for publications that describe randomized controlled trials (RCTs) of antifibrinolytic therapy in patients presenting with haemoptysis. We also performed an independent search in MEDLINE for relevant trials not yet included in CENTRAL or DARE. Searches are up to date to the 19th September 2016. We conducted electronic and manual searches of relevant national and international journals. We reviewed the reference lists of included studies to locate relevant randomized controlled trials (RCTs). An additional search was carried out to find unpublished RCTs. SELECTION CRITERIA: We included RCTs designed to evaluate the effectiveness and safety of antifibrinolytic agents in reducing haemoptysis in adult and paediatric patients of both genders presenting with haemoptysis of any etiology and severity. The intervention of interest was the administration of antifibrinolytic agents compared with placebo or no treatment. DATA COLLECTION AND ANALYSIS: All reviewers independently assessed methodological quality and extracted data tables pre-designed for this review. MAIN RESULTS: The electronic literature search identified 1 original study that met the eligibility criteria. One unpublished study was also identified through manual searches. Therefore two randomized controlled trials met the inclusion criteria: Tscheikuna 2002 (via electronic searches) and Ruiz 1994 (via manual searches). Tscheikuna 2002, a double-blind RCT performed in Thailand, evaluated the effectiveness of tranexamic acid (TXA, an antifibrinolytic agent) administered orally in 46 hospital in- and outpatients with haemoptysis of various etiologies. Ruiz 1994, a double-blind RCT performed in Peru, evaluated the effectiveness of intravenous TXA in 24 hospitalised patients presenting with haemoptysis secondary to tuberculosis.Pooled together, results demonstrated a significant reduction in bleeding time between patients receiving TXA and patients receiving placebo with a weighted mean difference (WMD) of -19.47 (95% CI -26.90 to -12.03 hours), but with high heterogeneity (I(2) = 52%). TXA did not affect remission of haemoptysis evaluated at seven days after the start of treatment. Adverse effects caused by the drug's mechanism of action were not reported. There was no significant difference in the incidence of mild side effects between active and placebo groups (OR 3.13, 95% CI 0.80 to 12.24). AUTHORS' CONCLUSIONS: There is insufficient evidence to judge whether antifibrinolytics should be used to treat haemoptysis from any cause, though limited evidence suggests they may reduce the duration of bleeding.

Internal Medicine

Siddiqui MA, Eraqi H, **Omar S**, and **Jafri SM**. Massive disparity in insurance approval; a comparison between ledipasvir/sofosbuvir based hepatitis C therapy and adalimumab based IBD therapy *Hepatology* 2016; 63(1):474A. PMID: Not assigned. Abstract

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Purpose: We evaluated the success rate for insurance approval for a single center setting for hepatitis C therapy involving ledipasvir/sofosbuvir and compared it to IBD therapy involving Adalimumab. Methods: Pharmaceutical records were reviewed for all patients prescribed ledipasvir/sofosbuvir and Adalimumab between July 2014 and November 2015. Data was extracted including type of insurance, insurance approval, fibrosis staging based on fibroscan for the patients who were prescribed ledipasvir/sofosbuvir and data for type of IBD, severity of anemia, location, extraintestinal manifestations and perianal complications was collected for the patients who were prescribed Adalimumab. Results: 783 patients were prescribed therapy with ledipasvir/sofosbuvir based therapy and the overall approval rate was 77.8%. In comparison ammong the 55 patients who were prescribed Adalimumab 52 (94.5%) were approved, 2 patients were denied and 1 was still pending approval. Among the patients who were prescribed ledipasvir/ sofosbuvir by insurance companies 296 patients (37.8%) had Medicare, 424 (54.1%) private insurance and (8.2%) had Medicaid. The approval rates were 93% for Medicare patients, 79% for private insurances and 32% for Medicaid patients. Amongst private insurances, Private A had approval rate of 87%, Private B had approval rate of 73% and other private insurances had approval of 71%. In the Adalimumab group, 7.3% patients had Medicare and Medicaid each, 14.6% patients had Private A, 69.1% had Private B and 1.8% had other private insurance. All the patients who had Medicaid or Medicare were approved. Of the 2 patients who were denied one had Private B, Crohn's disease as the diagnoses and absence of anemia or extraintestinal manifestations. Whereas the second patient had insurance other than Private A or B, Ulcerative colitis as the diagnoses, presence of moderate anemia and no extra-intestinal manifestations. Conclusion: We evaluated insurance approval rates of ledipasvir/ sofosbuvir based hepatitis C therapy and Adalimumab based IBD therapy. The over-all approval rate of therapy based on ledipasvir/sofosbuvir was 77.8% and Medicaid patients had a very low approval rate of 32%. The overall approval rate for Adalimumab based therapy was 94.5% and all the Medicare and Medicaid patients were approved. The only patients who were denied had private insurance. (Table Presented).

Medical Education

Aoun J, Shaw J, **Eisenstein D**, and Tsafrir Z. Long-term follow-up after surgical repair of occult hernia in women with unexplained chronic pelvic pain *J Minim Invasive Gynecol* 2016; 23(7):S237. PMID: Not assigned. Abstract

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Study Objective: To evaluate whether surgical repair of ultrasounddiagnosed occult hernia resulted in improvement of pain scores in a female clinic population with unexplained pelvic pain. Design: Retrospective cohort study with follow-up questionnaire. Setting: Pelvic pain clinic at a university-affiliated tertiary medical center in Southeast Michigan. Patients: Female patients with unexplained chronic pelvic pain who underwent surgical repair of ultrasound-diagnosed occult hernia between January 2005 and July 2012. Intervention: Patients were contacted for a follow-up interview 3 to 9 years after their procedure. Measurements and Main Results: Among 96 women with unexplained chronic pelvic pain and focal groin tenderness, 51 (53%) were positive for ultrasound-diagnosed occult hernia, of those, 35 (69%) were surgically repaired. Long-term follow-up after hernia repair was possible in 40% of patients, via phone interview. When the preoperative and postoperative scores were compared, the average pain improvement was 60% using the Brief Pain Inventory and 56% using the Short Form McGill Pain Questionnaire. Improvement was noted in all categories of the questionnaires. Sixty-four % (9/14) considered the surgery to be effective and 79% (11/14) were overall satisfied with the results, and finally, 71% (10/14) claimed that they would have the surgery again. No association was found between patients' satisfaction with their hernia repair surgery and co-morbidities such as smoking, hypertension, diabetes mellitus, degenerative joint disease, and obesity. Conclusion: The majority of women with ultrasound-diagnosed occult hernia reported improvement of their pain after surgical repair. Some women, however, did not or only partially benefited from the procedure, which illustrate the difficulties faced by practitioners in diagnosing and treating individual findings like occult hernia in chronic pelvic pain patients where etiologic multiplicity is not uncommon.

Neonatology

Rito DC, Viehl LT, Buchanan PM, Haridas S, and Koenig JM. Augmented th17-type immune responses in preterm neonates exposed to histologic chorioamnionitis *Pediatr Res* 2016;PMID: 27870827. Article Request Form

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Department of Molecular Microbiology & Immunology, Saint Louis University, St. Louis, MO.

BACKGROUND: Histologic chorioamnionitis (HCA) is a placental inflammatory disorder that frequently precedes preterm delivery. HCA increases risk for long-standing inflammatory injury and may influence immune programming, particularly in preterm (PT) neonates. We hypothesized that HCA exposure is associated with an increased circulating frequency of pro-inflammatory, Th17-type responses. METHODS: Placental cord blood was collected from HCA-exposed or control neonates (23-41 weeks gestation). Frequencies of Th17 and T regulatory (Treg) cells and assessments of Th17-type features in CD4 and Treg cells were determined by flow cytometric analysis. RESULTS: Cord blood samples from 31 PT and 17 term neonates were analyzed by flow cytometry. A diagnosis of HCA in extremely PT (EPT, GA </= 30 wk) gestations was associated with the highest cord blood frequencies of progenitor (pTh17, CD4+CD161+) and mature (mTh17, CD4+CD161+CCR6+) Th17 cells. Preterm neonates exposed to HCA also exhibited elevated cord blood frequencies of IL-17+ Treg cells, as well as T cells with effector memory phenotype (TEM) that co-expressed Th17-type surface antigens. CONCLUSION: Th17-type responses are amplified in preterm neonates exposed to HCA. We speculate that a Th17 bias may potentiate the inflammatory responses and related morbidity observed in preterm neonates whose immune systems have been 'primed' by HCA exposure.

Nephrology

Ishida JH, **Patel A**, Mehta AK, Gatault P, McBride JM, Burgess T, Derby MA, Snydman DR, Emu B, Feierbach B, Fouts AE, Maia M, Deng R, Rosenberger CM, Gennaro LA, Striano NS, Liao XC, and Tavel JA. Phase 2 randomized, double-blind, placebo-controlled trial of rg7667, a combination monoclonal antibody, for prevention of cytomegalovirus infection in high-risk kidney transplant recipients *Antimicrob Agents Chemother* 2016;PMID: 27872061. Full Text

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BACKGROUND: Cytomegalovirus (CMV) infection is a significant complication after kidney transplantation. We examined the ability of RG7667, a combination of two monoclonal antibodies, to prevent CMV infection in high-risk kidney transplant recipients in a randomized, double-blind, placebo-controlled trial. METHODS: CMV-seronegative recipients of a kidney transplant from a CMV-seropositive donor (D+R-) were randomized to receive RG7667 (n=60) or placebo (n=60) at the time of transplant, and 1, 4, and 8 weeks posttransplant. Patients were monitored for CMV viremia every 1-2 weeks posttransplant for 24 weeks. Patients who had seroconverted (D+R+) or withdrawn before dosing were excluded from the analysis (n=4). RESULTS: CMV viremia occurred in 27 of 59 (45.8%) patients receiving RG7667 and 35 of 57 (61.4%) patients receiving placebo (stratum-adjusted difference 15.3%; p = 0.100) within 12 weeks posttransplant and in 30 of 59 (50.8%) patients receiving RG7667 and 40 of 57 (70.2%) patients receiving placebo (stratum-adjusted difference 19.3%; p = 0.040) within 24 weeks posttransplant. Median time to CMV viremia was 139 days in patients receiving RG7667 compared to 46 days in patients receiving placebo (hazard ratio 0.53; p = 0.009). CMV disease was less common in the RG7667 than placebo group (3.4% versus 15.8%; p = 0.030). Adverse events were generally balanced between treatment groups. CONCLUSIONS: In high-risk kidney transplant recipients, RG7667 was well tolerated, numerically reduced the incidence of CMV infection within 12 and 24 weeks posttransplant, delayed time to CMV viremia, and was associated with less CMV disease compared to placebo.

Neurology

Gulyani S, Salas R, Mari Z, Choi S, **Mahajan A**, and Gamaldo C. Evaluating and managing sleep disorders in the parkinson's disease clinic *Basal Ganglia* 2016; 6(3):165-172. PMID: 27818912. Article Request Form

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Parkinson's disease is a multi-systems neurodegenerative disorder that is characterized by a combination of motor and non-motor symptoms. Non-motor symptoms of Parkinson's disease comprise a variety of cognitive, neuropsychiatric, autonomic, sensory, and sleep complaints. Although sleep disruption represents one of the most common non-motor symptom complaints among Parkinson's disease patients, recommendations regarding effective evaluation and management strategies for this specific population remain limited. This review gives an evidence based summary of the available treatment options and management strategies for the sleep complaints commonly encountered by patients with Parkinson's disease.

Neurology
Krisciunas GP, Castellano K, McCulloch TM, Lazarus CL, Pauloski BR, Meyer TK, Graner D, Van Daele DJ, **Silbergleit AK**, Crujido LR, Rybin D, Doros G, Kotz T, and Langmore SE. Impact of compliance on dysphagia rehabilitation in head and neck cancer patients: Results from a multi-center clinical trial *Dysphagia* 2016;PMID: 27848021. Full Text

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A 5-year, 16-site, randomized controlled trial enrolled 170 HNC survivors into active (estim + swallow exercise) or control (sham estim + swallowing exercise) arms. Primary analyses showed that estim did not enhance swallowing exercises. This secondary analysis determined if/how patient compliance impacted outcomes. A home program, performed 2 times/day, 6 days/week, for 12 weeks included stretches and 60 swallows paired with real or sham estim. Regular clinic visits ensured proper exercise execution, and detailed therapy checklists tracked patient compliance which was defined by mean number of sessions performed per week (0-12 times) over the 12-week intervention period. "Compliant" was defined as performing 10-12 sessions/week. Outcomes were changes in PAS, HNCI, PSS, OPSE, and hyoid excursion. ANCOVA analyses determined if outcomes differed between real/sham and compliant/noncompliant groups after 12 weeks of therapy. Of the 170 patients enrolled, 153 patients had compliance data. The mean number of sessions performed was 8.57/week (median = 10.25). Fifty-four percent of patients (n = 83) were considered "compliant." After 12 weeks of therapy, compliant patients in the sham estim group realized significantly better PAS scores than compliant patients in the active estim group (p = 0.0074). When pooling all patients together, there were no significant differences in outcomes between compliant and non-compliant patients. The addition of estim to swallowing exercises resulted in worse swallowing outcomes than exercises alone, which was more pronounced in compliant patients. Since neither compliant nor non-compliant patients benefitted from swallowing exercises, the proper dose and/or efficacy of swallowing exercises must also be questioned in this patient population.

Neurology
Mahajan A, Patel A, Nadkarni G, and **Sidiropoulos C**. Are hospitalized Parkinson's disease patients more likely to carry a do-not-resuscitate order? *J Clin Neurosci* 2016;PMID: 27810417. Full Text

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While DNR utilization is a complex subjective phenomenon, the effect of such a decision can collectively influence attitudes of care. The role of palliative care in advanced PD has been under appreciated. We reviewed the Healthcare Cost and Utilization Project's National Inpatient Sample (NIS) database from 2012 for all hospitalizations 65years. We identified PD by using ICD-9-CM code 332.0 and DNR status with ICD code - V49.86 entered during the

same admission as a secondary diagnosis. We estimated risk of mortality by the 3M All Patient Refined DRG (APR DRG) classification System and generated multivariate regression models to assess associations between DNR and PD after adjusting for confounders. Finally, we tested for interaction by risk of mortality. We analyzed 12,700,000 hospitalizations with age 65years in 2012, of which 246625 (1.94%) pts had PD. Proportion of DNR utilization was higher among PD patients vs. those without, 20895 (8.47%) vs. 723090 (5.8%) (p<0.01). In multivariable regression analysis, PD patients were associated with higher odds of DNR utilization [Adjusted Odds ratio (aOR): 1.26, 95% CI: 1.21, 1.30, p<0.001]. Finally, the odds of DNR utilization increased significantly with APR-DRG stage [aOR: 1 vs. 1.61 (Stage 2) vs. 2.46 (Stage 3) vs. 3.61 (Stage 4); p<0.0001]. PD patients have higher odds of DNR utilization than the general population, which worsens with increasing objective risk of mortality. This is likely correlated with perception of end of life and importance of QOL with increasing severity of overall illness.

Neurology

Marrotte EJ, **Mitsias P**, **Melvin L**, **Mahmood A**, **Tsivgoulis G**, and **Varelas P**. Real-time detection of cerebral artery rebleeding by transcranial doppler ultrasound: Hemodynamic changes and response to treatment *J Clin Neurol* 2016;PMID: 27868398. Full Text

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Neurology

Samudra N, **Patel N**, Womack KB, Khemani P, and Chitnis S. Psychosis in parkinson disease: A review of etiology, phenomenology, and management *Drugs Aging* 2016; 33(12):855-863. PMID: 27830568. Article Request Form

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Parkinson disease psychosis (PDP) is a common phenomenon in Parkinson disease (PD) patients treated with dopaminergic drugs, and is associated with high morbidity and mortality. It also correlates with depression and dementia, and can contribute to considerable caregiver stress and burnout. While symptoms can be relieved by decreasing doses or number of anti-PD medications, this may lead to an unacceptable worsening of motor function. When general medical or psychiatric conditions have been ruled out, and decreasing dopaminergic agents is not effective in treating psychosis, therapies include atypical antipsychotics, primarily clozapine and quetiapine. Of these, clozapine is effective but is associated with a poor side-effect profile and the necessity for frequent blood draws. Clinicians prefer quetiapine for its theoretically better safety profile, although there is no evidence for efficacy in treating psychosis. All atypical antipsychotics are associated with increased mortality in this patient population. Cholinesterase inhibitors can ameliorate psychosis symptoms. The serotonin 5-HT2A receptor inverse agonist pimavanserin was recently approved by the US FDA for the treatment of PDP and may prove to be a more targeted therapy without the downsides of atypical antipsychotics.

Neurology

Shah K, and **Miller DJ**. Three-dimensional modeling of Eagle syndrome *Neurology* 2016; 87(21):2279-2280. PMID: 27872222. Full Text

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Neurology

Shvarts V, Zoltay G, **Bowyer SM**, **Zillgitt A**, **Moran JE**, **Mason RK**, **Tepley N**, and Burdette D. Periodic discharges: Insight from magnetoencephalography *J Clin Neurophysiol* 2016;PMID: 27832046. Full Text

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PURPOSE: This study utilized magnetoencephalography (MEG) dipole localization and coherence measurement to evaluate the magnetic fields associated with periodic discharges. The primary goal of the study was to evaluate whether MEG could consistently localize quasiperiodic discharges that were observed on the EEG portion of the recording. The secondary objective was to evaluate whether coherence measurements would correlate with topographic maxima of epileptiform activity. METHODS: A total of 13 inpatients, whose electrographic records demonstrated lateralized periodic discharges (LPDs), were recruited from Henry Ford Hospital neurology and intensive care units. Nine patients were found clinically to be in status epilepticus prior to the EEG determination of LPDs. Spontaneous cortical brain activity was recorded with 148-channel MEG for 10 minutes. Data were sampled at 508Hz and DC-100Hz and filtered from 1 Hz to 40 Hz. Interictal events were imaged with single equivalent current dipole (ECD) localization. MEG coherence source imaging (MEG-CSI) analysis was performed and compared to the cortical topography of LPDs patterns and to the focal lesions seen on the MRI (9 patients) or CT (5 patients) imaging modalities. RESULTS: The morphology of periodic waveforms was similar between EEG and MEG portions of the study. In patients with substrate positivity on imaging studies, coherence analysis revealed a tendency for LPDs to arise from the interface between the lesion and the surrounding, uncompromised cortex rather than from the lesion itself. In non-lesional patients with recent status epilepticus, the localization of maximal coherence was in the temporal lobes. CONCLUSIONS: This study demonstrated that MEG is able to detect and localize LPDs arising from damaged and adjacent cortex. The MEG-CSI measurements also suggest the presence of epileptogenic networks perilesionally in cases with focal lesions on imaging. In patients without acute anatomic abnormality, the MEG coherence identified the epileptogenic networks in temporal lobe structures. MEG coherence source imaging may provide physicians with markers for differentiating between LPDs arising from acute injury currents versus LPDs arising from prolonged status epilepticus.

Neurology

Sood A, **Williamson SR**, and **Leavitt DA**. Neuroendocrine tumor of the ureter: A zebra among horses *J Endourol Case Rep* 2016; 2(1):204-208. PMID: 27868098. Full Text

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Primary neuroendocrine tumors of the upper urinary tract are extremely rare. We report a case of de novo small cell carcinoma of the ureter that presented masquerading as a distal ureteral stone. A 55-year-old lady presented to our clinic with 1 month history of right lower back pain and hematuria. Her history was notable for stage 1B mixed clear cell-endometroid cancer of the uterus status post radical abdominal hysterectomy with adjuvant radiotherapy, 7 years before the current episode. The patient had no evidence of recurrence. Initial noncontrast imaging suggested a 2.5 mm calculus in the distal right ureter and hydronephrosis; however, ureteroscopy revealed a large fleshy mass at the location. Histopathologic evaluation demonstrated the lesion to be primary small cell carcinoma of the ureter, without evidence of it being a derivative of the prior gynecologic malignancy. Metastatic work-up revealed high burden retroperitoneal adenopathy. The patient was started on Cisplatin-based neoadjuvant chemotherapy with plan for nephroureterectomy in the future. At 3 months follow-up, the patient was doing well with significant shrinkage of retroperitoneal adenopathy and no evidence of disease progression.

Neurology

Yadav VN, Zamler D, Baker GJ, Kadiyala P, Erdreich-Epstein A, **DeCarvalho AC**, **Mikkelsen T**, Castro MG, and Lowenstein PR. CXCR4 increases in-vivo glioma perivascular invasion, and reduces radiation induced apoptosis: A genetic knockdown study *Oncotarget* 2016;PMID: 27863376. Full Text

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Glioblastoma (GBM) is a highly invasive brain tumor. Perivascular invasion, autovascularization and vascular co-option occur throughout the disease and lead to tumor invasion and progression. The molecular basis for perivascular invasion, i.e., the interaction of glioma tumor cells with endothelial cells is not well characterized. Recent studies indicate that glioma cells have increased expression of CXCR4. We investigated the in-vivo role of CXCR4 in

perivascular invasion of glioma cells using shRNA-mediated knock down of CXCR4. We show that primary cultures of human glioma stem cells HF2303 and mouse glioma GL26-Cit cells exhibit significant migration towards human (HBMVE) and mouse (MBVE) brain microvascular endothelial cells. Blocking CXCR4 on tumor cells with AMD3100 in-vitro, inhibits migration of GL26-Cit and HF2303 toward MBVE and HBMVE cells. Additionally, genetic down regulation of CXCR4 in mouse glioma GL26-Cit cells inhibits their in-vitro migration towards MBVE cells; in an in-vivo intracranial mouse model, these cells display reduced tumor growth and perivascular invasion, leading to increased survival. Quantitative analysis of brain sections showed that CXCR4 knockdown tumors are less invasive. Lastly, we tested the effects of radiation on CXCR4 knock down GL26-Cit cells in an orthotopic brain tumor model. Radiation treatment increased apoptosis of CXCR4 downregulated tumor cells and prolonged median survival. In summary, our data suggest that CXCR4 signaling is critical for perivascular invasion of GBM cells and targeting this receptor makes tumors less invasive and more sensitive to radiation therapy. Combination of CXCR4 knock down and radiation treatment might improve the efficacy of GBM therapy.

Neurology

Yu X, Yuan L, Jackson A, Sun J, Huang P, Xu X, Mao Y, Lou M, **Jiang Q**, and Zhang M. Prominence of medullary veins on susceptibility-weighted images provides prognostic information in patients with subacute stroke *AJNR Am J Neuroradiol* 2016; 37(3):423-429. PMID: 26514606. Full Text

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BACKGROUND AND PURPOSE: The demonstration of prominent medullary veins in the deep white matter ipsilateral to acute ischemic stroke has been shown to predict poor clinical outcome. We have investigated the prognostic implications of prominent medullary veins in patients with subacute stroke who present outside the therapeutic window for revascularization therapy. MATERIALS AND METHODS: Forty-three consecutive patients with ischemic stroke in the middle cerebral artery territory presenting within 3-7 days of ictus were enrolled. The presence of prominent medullary veins in the periventricular white matter of the ipsilateral and contralateral medullary vein hemispheres was recorded. Perfusion-weighted imaging was used to calculate differences in hemispheric CBF from corresponding areas. Clinical outcome was classified as good if the modified Rankin Scale score was <3. RESULTS: Prominent medullary veins were observed in 24/43 patients with 14 ipsilateral medullary veins and 10 contralateral medullary veins. The ipsilateral medullary vein was independently associated with poor outcome (odds ratio, 11.19; P = .046). The contralateral medullary vein was not independently predictive of outcome but was significantly more common in patients with good outcome (90.0% contralateral medullary veins). A mean 64.5% decrease and a 52.4% increase of differences in hemispheric CBF were found in ipsilateral medullary veins and contralateral medullary veins, respectively. CONCLUSIONS: The ipsilateral medullary vein was a significant predictive biomarker of poor clinical outcome after stroke and was associated with hypoperfusion. The contralateral medullary vein was associated with good clinical outcome, and we hypothesize that prominent contralateral medullary veins indirectly reflect increased CBF in the ipsilateral hemisphere due to spontaneous recanalization or collateral flow.

Neurology

Yuan L, Yu X, Zhang M, **Jiang Q**, and P. Du Y. Correction of t1 effects in calculation of relative recirculation in ischemic stroke patients *Journal of Medical and Biological Engineering* 2016; 36(5):740-750. PMID: Not assigned. Article Request Form

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Relative recirculation (rR) is a promising surrogate permeability biomarker derived from dynamic susceptibility contrast (DSC) magnetic resonance imaging (MRI), and can be applied to predict hemorrhagic transformation (HT). However, the influence of T1 effects on the calculation of rR has not been properly investigated. Furthermore, a correction method for T1 effects in rR calculation has not been reported. In this study, a two-compartment model is used to simulate the influence of T1 effects on rR under various imaging conditions. The results of the simulation demonstrate that the rR values calculated with T1 effects are smaller than, or even have the opposite sign, compared to those calculated without T1 effects. Data of 17 DSC–MRI scans were obtained from 14 ischemic stroke patients

known to have blood–brain barrier (BBB) disruption on post-contrast T1-weighted images. A method is proposed to correct the T1 effects in the calculation of rR, and applied to analyze the ischemic stroke patient dataset. The statistics from an in vivo study show that the corrected rR in BBB disruption regions is significantly higher than the uncorrected rR ($p < 0.05$). Specifically, the corrected rR is positive, whereas the uncorrected rR is negative. rR values calculated without removing T1 effects can be severe underestimations. Using the proposed T1 correction method, the obtained rR can be adjusted to a level in accordance with known vascular physiology. As a semi-quantitative biomarker, rR with a high accuracy can potentially improve clinical assessment, such as the prediction of HT.

Neurosurgery

John JK, **Robin AM**, **Pabaney AH**, **Rammo RA**, **Schultz LR**, **Sadry NS**, and **Lee IY**. Complications of ventricular entry during craniotomy for brain tumor resection *J Neurosurg* 2016:1-7. PMID: 27813467. Full Text

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OBJECTIVE Recent studies have demonstrated that periventricular tumor location is associated with poorer survival and that tumor location near the ventricle limits the extent of resection. This finding may relate to the perception that ventricular entry leads to further complications and thus surgeons may choose to perform less aggressive resection in these areas. However, there is little support for this view in the literature. This study seeks to determine whether ventricular entry is associated with more complications during craniotomy for brain tumor resection. METHODS A retrospective analysis of patients who underwent craniotomy for tumor resection at Henry Ford Hospital between January 2010 and November 2012 was conducted. A total of 183 cases were reviewed with attention to operative entry into the ventricular system, postoperative use of an external ventricular drain (EVD), subdural hematoma, hydrocephalus, and symptomatic intraventricular hemorrhage (IVH). RESULTS Patients in whom the ventricles were entered had significantly higher rates of any complication (46% vs 21%). Complications included development of subdural hygroma, subdural hematoma, intraventricular hemorrhage, subgaleal collection, wound infection, urinary tract infection/deep venous thrombosis, hydrocephalus, and ventriculoperitoneal (VP) shunt placement. Specifically, these patients had significantly higher rates of EVD placement (23% vs 1%, $p < 0.001$), hydrocephalus (6% vs 0%, $p = 0.03$), IVH (14% vs 0%, $p < 0.001$), infection (15% vs 5%, $p = 0.04$), and subgaleal collection (20% vs 4%, $p < 0.001$). It was also observed that VP shunt placement was only seen in cases of ventricular entry (11% vs 0%, $p = 0.001$) with 3 of 4 of these patients having a large ventricular entry (defined here as entry greater than a pinhole [< 3 mm] entry). Furthermore, in a subset of glioblastoma patients with and without ventricular entry, Kaplan-Meier estimates for survival demonstrated a median survival time of 329 days for ventricular entry compared with 522 days for patients with no ventricular entry (HR 1.13, 95% CI 0.65-1.96; $p = 0.67$). CONCLUSIONS There are more complications associated with ventricular entry during brain tumor resection than in nonviolated ventricular systems. Better strategies for management of periventricular tumor resection should be actively sought to improve resection and survival for these patients.

Neurosurgery

Lee I, **Kalkanis S**, and Hadjipanayis CG. Stereotactic laser interstitial thermal therapy for recurrent high-grade gliomas *Neurosurgery* 2016; 79 Suppl 1:S24-s34. PMID: 27861323. Full Text

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BACKGROUND: The value of maximal safe cytoreductive surgery in recurrent high-grade gliomas (HGGs) is gaining wider acceptance. However, patients may harbor recurrent tumors that may be difficult to access with open surgery. Laser interstitial thermal therapy (LITT) is emerging as a technique for treating a variety of brain pathologies, including primary and metastatic tumors, radiation necrosis, and epilepsy. OBJECTIVE: To review the role of LITT in the treatment of recurrent HGGs, for which current treatments have limited efficacy, and to discuss the possible role of LITT in the disruption of the blood-brain barrier to increase delivery of chemotherapy locoregionally. METHODS: A MEDLINE search was performed to identify 17 articles potentially appropriate for review. Of these 17, 6 reported currently commercially available systems and as well as magnetic resonance thermometry to monitor the ablation and, thus, were thought to be most appropriate for this review. These studies were then reviewed for complications associated with LITT. Ablation volume, tumor coverage, and treatment times were also reviewed. RESULTS: Sixty-four lesions in 63 patients with recurrent HGGs were treated with LITT. Frontal (n = 34), temporal (n = 14), and parietal (n = 16) were the most common locations. Permanent neurological deficits were seen in 7 patients (12%), vascular injuries occurred in 2 patients (3%), and wound infection was observed in 1 patient (2%). Ablation coverage of the lesions ranged from 78% to 100%. CONCLUSION: Although experience using LITT for recurrent HGGs is growing, current evidence is insufficient to offer a recommendation about its role in the treatment paradigm for

recurrent HGGs. ABBREVIATIONS: BBB, blood-brain barrierFDA, US Food and Drug AdministrationGBM, glioblastoma multiformeHGG, high-grade gliomaLITT, laser interstitial thermal therapy.

Neurosurgery
Macki M, and **Dabaja AA**. Literature review of vaccine-related adverse events reported from HPV vaccination in randomized controlled trials *Basic Clin Androl* 2016; 26:16. PMID: 27895921. Full Text

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BACKGROUND: The human papilloma virus (HPV) infections were addressed with two FDA-approved HPV vaccines: quadrivalent and bivalent vaccine. The objective of this manuscript is to determine the safety of the HPV vaccine. RESULTS: A search of PubMed articles for "human papillomavirus vaccine" was used to identify all-type HPV clinical studies prior to October 2014. A refined search of clinical trials, multicenter studies, and randomized studies were screened for only randomized controlled trials comparing HPV vaccine to controls (saline placebo or aluminum derivatives). Studies were limited to the two FDA-approved vaccines. Following PRISMA guidelines, the literature review rendered 13 publications that met inclusion/ exclusion criteria. Gender was limited to females in 10 studies and males in 1 study. Two studies included both males and females. Of the 11,189 individuals in 7 publications reporting cumulative, all-type adverse events (AE), the AE incidence of 76.52 % (n = 4544) in the vaccinated group was statistically significantly higher than 67.57 % (n = 3548) in the control group ($p < 0.001$). The most common AE were injection-site reactions. On the other hand, systemic symptoms did not statistically significantly differ between the vaccination cohort (35.28 %, n = 3351) and the control cohort (36.14 %, n = 3198) ($p = 0.223$). The pregnancy/ perinatal outcomes rendered no statistically significant difference between the vaccine group and control group. CONCLUSION: Because the statistically significantly higher incidence of AE in the HPV vaccine group was primarily limited to injection-site reactions, the vaccinations are safe preventative measures in both males and females.

Neurosurgery
Marrotte EJ, **Mitsias P**, **Melvin L**, **Mahmood A**, **Tsivgoulis G**, and **Varelas P**. Real-time detection of cerebral artery rebleeding by transcranial doppler ultrasound: Hemodynamic changes and response to treatment *J Clin Neurol* 2016;PMID: 27868398. Full Text

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Neurosurgery
Yadav VN, Zamler D, Baker GJ, Kadiyala P, Erdreich-Epstein A, **DeCarvalho AC**, **Mikkelsen T**, Castro MG, and Lowenstein PR. CXCR4 increases in-vivo glioma perivascular invasion, and reduces radiation induced apoptosis: A genetic knockdown study *Oncotarget* 2016;PMID: 27863376. Full Text

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Glioblastoma (GBM) is a highly invasive brain tumor. Perivascular invasion, autovascularization and vascular co-option occur throughout the disease and lead to tumor invasion and progression. The molecular basis for perivascular invasion, i.e., the interaction of glioma tumor cells with endothelial cells is not well characterized. Recent studies indicate that glioma cells have increased expression of CXCR4. We investigated the in-vivo role of CXCR4 in perivascular invasion of glioma cells using shRNA-mediated knock down of CXCR4. We show that primary cultures of human glioma stem cells HF2303 and mouse glioma GL26-Cit cells exhibit significant migration towards human (HBMVE) and mouse (MBVE) brain microvascular endothelial cells. Blocking CXCR4 on tumor cells with AMD3100 in-vitro, inhibits migration of GL26-Cit and HF2303 toward MBVE and HBMVE cells. Additionally, genetic down regulation of CXCR4 in mouse glioma GL26-Cit cells inhibits their in-vitro migration towards MBVE cells; in an in-vivo intracranial mouse model, these cells display reduced tumor growth and perivascular invasion, leading to increased survival. Quantitative analysis of brain sections showed that CXCR4 knockdown tumors are less invasive. Lastly, we

tested the effects of radiation on CXCR4 knock down GL26-Cit cells in an orthotopic brain tumor model. Radiation treatment increased apoptosis of CXCR4 downregulated tumor cells and prolonged median survival. In summary, our data suggest that CXCR4 signaling is critical for perivascular invasion of GBM cells and targeting this receptor makes tumors less invasive and more sensitive to radiation therapy. Combination of CXCR4 knock down and radiation treatment might improve the efficacy of GBM therapy.

Obstetrics, Gynecology and Women's Health Services

Aoun J, Shaw J, **Eisenstein D**, and Tsafrir Z. Long-term follow-up after surgical repair of occult hernia in women with unexplained chronic pelvic pain *J Minim Invasive Gynecol* 2016; 23(7):S237. PMID: Not assigned. Abstract

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Study Objective: To evaluate whether surgical repair of ultrasounddiagnosed occult hernia resulted in improvement of pain scores in a female clinic population with unexplained pelvic pain. Design: Retrospective cohort study with follow-up questionnaire. Setting: Pelvic pain clinic at a university-affiliated tertiary medical center in Southeast Michigan. Patients: Female patients with unexplained chronic pelvic pain who underwent surgical repair of ultrasound-diagnosed occult hernia between January 2005 and July 2012. Intervention: Patients were contacted for a follow-up interview 3 to 9 years after their procedure. Measurements and Main Results: Among 96 women with unexplained chronic pelvic pain and focal groin tenderness, 51 (53%) were positive for ultrasound-diagnosed occult hernia, of those, 35 (69%) were surgically repaired. Long-term follow-up after hernia repair was possible in 40% of patients, via phone interview. When the preoperative and postoperative scores were compared, the average pain improvement was 60% using the Brief Pain Inventory and 56% using the Short Form McGill Pain Questionnaire. Improvement was noted in all categories of the questionnaires. Sixty-four % (9/14) considered the surgery to be effective and 79% (11/14) were overall satisfied with the results, and finally, 71% (10/14) claimed that they would have the surgery again. No association was found between patients' satisfaction with their hernia repair surgery and co-morbidities such as smoking, hypertension, diabetes mellitus, degenerative joint disease, and obesity. Conclusion: The majority of women with ultrasound-diagnosed occult hernia reported improvement of their pain after surgical repair. Some women, however, did not or only partially benefited from the procedure, which illustrate the difficulties faced by practitioners in diagnosing and treating individual findings like occult hernia in chronic pelvic pain patients where etiologic multiplicity is not uncommon.

Obstetrics, Gynecology and Women's Health Services

Aoun J, Shaw J, **Eisenstein D**, and Tsafrir Z. Diagnosis of occult hernia in women with unexplained chronic pelvic pain *J Minim Invasive Gynecol* 2016; 23(7):S15. PMID: Not assigned. Abstract

J. Aoun, Ob/Gyn/MIGS, Henry Ford Hospital, West Bloomfield, United States

Study Objective: To determine the frequency of ultrasound diagnosis of occult hernia in a female clinic population with unexplained pelvic pain. Design: Retrospective cohort study (Canadian Task Force classification II-3). Setting: Pelvic pain clinic at a university-affiliated tertiary medical center in Southeast Michigan. Patients: Female patients with unexplained chronic pelvic pain and physical exam positive for focal groin tenderness without evidence of hernia seen between January 2005 and July 2012. Intervention: Patients underwent a standardized ultrasound of the inguinal and upper thigh soft tissue anatomy at rest and with provocative maneuvers. A single provider performed all ultrasounds. Measurements and Main Results: A total of 96 women were included. Fifty-one patients (53%) had an ultrasound suggestive of occult hernia. Among them eight patients had two hernias. Sixty-three percent were inguinal hernias (51% direct and 12% indirect), 29% were femoral, 5% spigelian, and 2% umbilical. All patients with positive ultrasound findings were referred to general surgery. Sixty-nine percent of patients (35/51) underwent surgical evaluation. The ultrasound diagnosis of occult hernia was correctly confirmed surgically in 97% of patients (34/35). Patients who underwent surgical repair had higher pain metrics on their Brief Pain Inventory ($p = 0.01$). Patients with unexplained pelvic pain and evidence of occult hernia on ultrasound were significantly older (41 years vs 34 years, respectively, $p = 0.005$) and more likely to have a history of arthritis as compared to patients with similar pain profile and without evidence of hernia on ultrasound ($p = 0.02$). Conclusion: In this retrospective analysis of women with unexplained chronic pelvic pain and focal groin tenderness, we found evidence to support that the diagnosis of hernia on soft tissue ultrasound was found in half of the cases, and that such results were highly correlated with surgical findings.

Obstetrics, Gynecology and Women's Health Services

Bazzi M, **Abdullah N**, **Karabon P**, Chick J, and **Dabaja AA**. Trends in embryo transfer rate, multiple birth rate, and pregnancy rate in response to the american society of reproductive medicine's recommendation to limit embryotransfer *Fertility and Sterility* 2016; 106:e325. PMID: Not assigned. Abstract

M. Bazzi, Wayne State University, School of Medicine, Dearborn, United States

OBJECTIVE: Multiple embryo transfer during in vitro fertilization (IVF) can lead to higher order pregnancy, and can complicate fetal and maternal health. The American Society for Reproductive Medicine (ASRM) passed recommendation in 1977 to reduce the number of embryos transferred during IVF. We evaluated the long-term impact of ASRM's recommendation on embryo transfer rate (ETR), multiple birth rate (MBR), and pregnancy rate (PR) from 1997 to 2012. DESIGN: Retrospective analysis of previously published ETR. MATERIALS AND METHODS: Using publicly available data from the Centers for Disease Control and Prevention (CDC), we calculated the national ETR, MBR, and PR for a given year. The fertility success reports provided data stratified by the following age groups: less than 35 years old, between 35 and 40 years old and greater than 40 years old. For statistical analysis, we used a multilevel linear mixed effects model to assess temporal/ time trends. Temporal trends were tested using the Estimated Annual Percentage Change (EAPC) methodology. All statistical analysis was performed using SAS 9.4 (Cary, North Carolina; SAS Institute). RESULTS: Analyses from our study showed that the estimated annual percent change in embryo transfer rate and multiple birth rate is -3.36% and -1.90%, respectively (p-value <0.01) from 1997 to 2012. The pregnancy rate has improved between 1997 and 2012 with an estimated average percent change of 1.90% (p-value <0.01). CONCLUSIONS: Professional societies' recommendation to reduce the number of embryos transferred has effectively reduced national embryo transfer rate without compromising pregnancy rates.

Obstetrics, Gynecology and Women's Health Services

Eisenstein DI. Laparoscopic ultrasound during robotic myomectomy *J Minim Invasive Gynecol* 2016; 23(7):S118. PMID: Not assigned. Abstract

D.I. Eisenstein, Division of Minimally Invasive Gynecology, Department of Women's Health, Henry Ford Health System, W Bloomfield, United States

Robotic Myomectomy is primarily a visual surgical dissection without haptics. Ascertainment of multiple fibroids during myomectomy can therefore be challenging. Comparative studies of pre operative imaging versus intra operative ultrasound scanning with a laparoscopic probe demonstrate the superiority of laparoscopic ultrasound over MRI or standard ultrasound in defining number and location of fibroids. This video demonstrates the utility of laparoscopic ultrasound during robotic myomectomy in guiding dissection and removal of challenging multiple fibroids.

Obstetrics, Gynecology and Women's Health Services

Hijaz M, **Jankowski J**, and **Sangha R**. Factors affecting recurrence of leiomyomas in older women (above age 40) *J Minim Invasive Gynecol* 2016; 23(7):S13. PMID: Not assigned. Abstract

M. Hijaz, Henry Ford Hospital, Detroit, United States

Study Objective: To evaluate the association between route of surgery and myoma weight and recurrence of leiomyomas following myomectomy in women aged 40 and above. Design: A retrospective chart review. Setting: Academic affiliated community hospital: Henry Ford Health System. Patients: 64 women above the age of 40 who underwent uterine myomectomy, regardless of route, between 2003 and 2013. Intervention: Uterine myomectomy, regardless of route (open, robotic, laparoscopic, hysteroscopic). Measurements and Main Results: Atotal of 64 patients age above 40 were evaluated. 23 were open surgeries, 22 were laparoscopic/robotically, 10 hysteroscopically and 9 vaginally. A logistic regression model using route was used to predict recurrence. The open route was used as reference and the recurrence in other routes was compared. There was no association of route of surgery with recurrence (p 0.438). These women were followed for over a 10 year period. Recurrence was evaluated based on leiomyoma weight. Binary logistic regression model using myoma weight to predict recurrence was used. Odds ratio was scaled to 100 grams increase in myoma weight. In this patient population followed over a 10-year period, we noted that for every 100 grams increase in myoma weight, the odds of having a recurrence increased by 25% (OR 1.25, p 0.028). Conclusion: Recurrence is not associated with route of myomectomy in women aged 40 and older. Fibroid recurrence is associated with increasing fibroid weight. This would play a role in preoperative counseling those patient with large or multiple uterine fibroids.

Obstetrics, Gynecology and Women's Health Services

Hijaz M, **Jankowski J**, and **Sangha R**. Is race and BMI associated with leiomyoma recurrence in women above age 40? *J Minim Invasive Gynecol* 2016; 23(7):S241. PMID: Not assigned. Abstract

M. Hijaz, Henry Ford Hospital, Detroit, United States

Study Objective: To evaluate the association between race and recurrence of leiomyomas following myomectomy in women aged 40 and above. Design: A retrospective chart review. Setting: Academic affiliated community hospital: Henry Ford Health System Patients: 61 women above the age of 40 who underwent uterine myomectomy, regardless of route, between 2003 and 2013. Intervention: Uterine myomectomy, regardless of route (open, robotic, laparoscopic, hysteroscopic). Measurements and Main Results: A total of 61 patients were identified, 46 were African American, 6 were Caucasian, 3 Hispanic and 6 were classified as "other." Fisher's exact test was used to test for an association between race and recurrence. Results revealed p value of 0.606 showing non-significance. The mean BMI was 28.2 with S. D of 5.01 overall. There was no significant difference between the recurrence and no recurrence groups (p-value 0.438). Conclusion: There was no evidence of an association between race or BMI with recurrence in our patient population.

Obstetrics, Gynecology and Women's Health Services

Isrow D, **Burmeister C**, **Hanna RK**, and **Elshaikh MA**. Survival endpoints for young women with early stage uterine endometrioid carcinoma: a matched analysis *Eur J Obstet Gynecol Reprod Biol* 2016; 207:115-120. PMID: 27838535. Full Text

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OBJECTIVES: Younger age is thought to be a favorable prognostic factor in women with endometrial carcinoma (EC). Survival endpoints were compared between two matched groups of patients with early stage EC: women 45 years or younger and women older than 45 years. METHODS AND MATERIALS: Two matched groups of patients were created based on stage, grade, lymph node dissection and adjuvant management. Recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) were calculated. RESULTS: A total of 525 patients (88 younger patients and 437 older patients, matched 1:5) were included in this study. The two groups were well balanced except for less myometrial invasion in the younger patients. There were no significant differences between younger and older patients in regards to 5-year RFS (94% vs. 91%, p=0.6902). Similarly, there was no significant difference in regards to DSS (96% vs. 97%, p=0.9000). While 5-year OS was similar for both groups (89% vs. 89%, p=0.9942), 10-year OS was longer in the younger group (83% vs. 68% with p=0.13). On multivariate analysis for RFS, the presence of lymphovascular space invasion was the only predictor of shorter RFS (p=0.0007). Tumor grade (p=0.0002) and lower uterine segment involvement (p=0.0141) were independent predictors of shorter DSS. Older age (p<0.001) and stage II (p=0.01) were the only predictors of shorter OS. CONCLUSIONS: When matched based on tumor stage, grade and adjuvant management, our study suggests that there is no difference in survival endpoints between younger and older patients with early stage endometrial carcinoma.

Obstetrics, Gynecology and Women's Health Services

Ondersma SJ, Beatty JR, Rosano TG, **Strickler RC**, Graham AE, and Sokol RJ. Commercial ethyl glucuronide (etg) and ethyl sulfate (ets) testing is not vulnerable to incidental alcohol exposure in pregnant women *Subst Use Misuse* 2016; 51(1):126-130. PMID: 26771303. Article Request Form

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BACKGROUND: Ethyl Glucoronide (EtG) and Ethyl Sulfate (EtS) have shown promise as biomarkers for alcohol and may be sensitive enough for use with pregnant women in whom even low-level alcohol use is important. However, there have been reports of over-sensitivity of EtG and EtS to incidental exposure to sources such as alcohol-based

hand sanitizer. Further, few studies have evaluated these biomarkers among pregnant women, in whom the dynamics of these metabolites may differ. OBJECTIVES: This study evaluated whether commercial EtG-EtS testing was vulnerable to high levels of environmental exposure to alcohol in pregnant women. METHODS: Two separate samples of five nurses-one pregnant and the other postpartum, all of whom reported high levels of alcohol-based hand sanitizer use-provided urine samples before and 4-8 hours after rinsing with alcohol-based mouthwash and using hand sanitizer. The five pregnant nurses provided urine samples before, during, and after an 8-hour nursing shift, during which they repeatedly cleansed with alcohol-based hand sanitizer (mean 33.8 uses). The five postpartum nurses used hand sanitizer repeatedly between baseline and follow-up urine samples. RESULTS: No urine samples were positive for EtG-EtS at baseline or follow-up, despite use of mouthwash and-in the pregnant sample-heavy use of hand sanitizer (mean of 33.8 uses) throughout the 8-hour shift. CONCLUSIONS/IMPORTANCE: Current, commercially available EtG-EtS testing does not appear vulnerable to even heavy exposure to incidental sources of alcohol among pregnant and postpartum women.

Obstetrics, Gynecology and Women's Health Services

Petersen S, **Khangura R**, and **Sangha R**. Chorangiosis: Clinical associations and obstetrical outcomes *Obstet Gynecol* 2016; 127:131S-132S. PMID: Not assigned. Abstract

S. Petersen, Henry Ford Hospital, Detroit, United States

INTRODUCTION: A 38-year old Class C diabetic at 36w4d was taken for urgent c-section after non-stress testing revealed Category 3 fetal heart tones. At the time of delivery, a dusky umbilical cord suggestive of thrombosis was noted. Placental pathology revealed 40% occlusion of umbilical vein and chorangiosis. Chorangiosis is a vascular change of the placenta involving terminal chorionic villi, proposed to result from longstanding, low-grade hypoxia in placental tissue. It has been associated with diabetes, intrauterine growth restriction (IUGR), and hypertensive conditions. Clinical significance has not been studied extensively but case reports suggest correlation with increased fetal morbidity and mortality. METHODS: We identified 56 cases of "chorangiosis" on placental pathology at Henry Ford Hospital from 2010-2015. We reviewed factors such as: maternal age, BMI, smoking status, maternal health conditions, antenatal fetal issues, gestational age, mode of delivery and fetal outcome. RESULTS: Average age was 27.6 years; 20% of advanced maternal age. 16% of cases associated with hypertensive disorders, 11% with diabetes, 11% with IUGR and 45% associated with maternal obesity. 30% associated with current or former smokers. One resulted in neonatal death, 1 intrauterine fetal demise and 18% of deliveries were pre-term. 52% of deliveries were by cesarean section, with the most noted indication being abnormal fetal heart tones. CONCLUSION: Chorangiosis may contribute to increased rates of cesarean section due to abnormal fetal heart tones from longstanding hypoxia coupled with the stress of labor. Further studies are needed to characterize the association of chorangiosis with subsequent infant health outcomes.

Obstetrics, Gynecology and Women's Health Services

Petersen S, **Rubinfeld I**, **Buekers T**, and **Sangha R**. Analysis of risk factors for urologic injuries after minimally invasive vs abdominal hysterectomy *J Minim Invasive Gynecol* 2016; 23(7):S29. PMID: Not assigned. Abstract

S. Petersen, Henry Ford Hospital, Detroit, United States

Study Objective: To determine risk factors for urologic injury in patients undergoing hysterectomy. Design: Retrospective cohort study. Setting: Academic Affiliated Community Hospital System. Patients: All patients undergoing minimally invasive and abdominal hysterectomy between August 2013 and March 2016, after the institution of an electronic medical record. Intervention: Hysterectomy. Measurements and Main Results: A total of 2553 hysterectomies were identified. A total of 1814 minimally invasive, and 736 abdominal hysterectomies were analyzed for urologic complications. Rate of urologic injury was 0.95% for abdominal hysterectomy vs 0.83% minimally invasive hysterectomy (p value = 0.75). Intraoperative recognition of injury was 0.81% in open cases vs 0.61% in MIS case (p value = 0.55) . BMI was 32.5 for open vs 32.0 for MIS (p value = 0.22). BMI of injured patients was 33.7 vs 32.1 for non injured (p value =0.35). 67% of patients with injuries after minimally invasive hysterectomy had prior abdominal surgeries, whereas 50% of patients with injuries after abdominal hysterectomy had prior abdominal surgery. 17% vs 30% of patients with injuries after minimally invasive hysterectomy and abdominal hysterectomy respectively had endometriosis. Cystoscopy was completed in 83% of patients with urologic injury after minimally invasive surgery. Conclusion: Rates of urologic injury at our institution is similar to published data. Body mass index was not a significantly different in patients who had urologic injuries versus those who did not. Intraoperative recognition of injury was higher in abdominal hysterectomy than MIS, however, majority of injuries were diagnosed in the immediate postoperative period.

Obstetrics, Gynecology and Women's Health Services

Petersen S, and **Sangha R**. Urinary tract fistula after minimally invasive hysterectomy: Presentation and outcomes *J Minim Invasive Gynecol* 2016; 23(7):S218. PMID: Not assigned. Abstract

S. Petersen, Obstetrics and Gynecology, Henry Ford Hospital, Detroit, United States

Study Objective: To describe the presentation and long term outcomes of urinary tract fistulas, an uncommon complication of minimally invasive hysterectomy. Design: Case Report. Setting: Academic Affiliated Community Hospital System Patients: Women who underwent a minimally invasive hysterectomy between August 2013 to March 2016. Review of these 1814 charts revealed two cases of urinary tract fistulas. Intervention: Minimally Invasive Hysterectomy. Measurements and Main Results: Herewe describe the twocases of urinary tract fistulas after a robotic-assisted radical hysterectomy and a laparoscopic assisted vaginal hysterectomy. The rate of fistula formation was 0.001%. Bilateral ureteric injury after robotic type III radical hysterectomy presented 2-weeks post operatively as urosepsis and leakage of urine vaginally. CT Urogram confirmed ureterovaginal fistula, which was managed with bilateral ureteral stenting and eventual ureteral re-implantation 23 days after hysterectomy. Long-term outcome after repair include recurrent pyelonephritis and voiding dysfunction. The other patient underwent a laparoscopic assisted vaginal hysterectomy complicated by an intra-operatively diagnosed posterior bladder laceration, repaired primarily by urology. She presented 4-weeks postoperatively with vaginal leakage of urine. Cystogram confirmed vesicovaginal fistula. The vesicovaginal fistula was managed with Latzko repair per urogynecology 56 days after hysterectomy. Outcome after injury includes asymptomatic vesicoureteral. Conclusion: Urinary tract fistula is an uncommon complication after hysterectomy. Diagnosis and treatment of urinary tract injury at the time of hysterectomy is imperative, but may not always prevent fistula formation. Even with successful repair, patients continue to have longterm urologic dysfunction sequelae.

Obstetrics, Gynecology and Women's Health Services

Sangha R, **Bossick A**, and **Wegienka G**. Use of focus groups to identify pre-and post-hysterectomy patient centered preferences *J Minim Invasive Gynecol* 2016; 23(7):S241. PMID: Not assigned. Abstract

R. Sangha, Obstetrics and Gynecology, Henry Ford Hospital, Detroit, United States

Study Objective: To identify patient-centered preferences before hysterectomy, and to assess women's overall experience post-surgery. Design: Focus groups. Setting: Henry Ford Hospital (Detroit, MI) Patients: All English-speaking Henry Ford Health System patients having undergone hysterectomy and within three time periods post hysterectomy: 0-6 months, 6-12 months, 12 months and greater post hysterectomy. Intervention: Focus groups were conducted to identify women's expectations and degree to which patient-centered preferences were discussed before their hysterectomy surgeries, and to assess women's outcomes and overall experience post-surgery. Measurements and Main Results: A total of 25 women participated. Questions also addressed experiences and resources that helped to inform women's decisions to move forward with surgery, their reflections postsurgery, and advice participants had for women who might be facing a decision about hysterectomy. Women's expectations are illustrated in Table 1. The only expectation that persisted during recovery, regardless of the complications experienced, was that women thought they would heal faster and be back to their normal energy level than the doctor predicted Women brought up the following topics that they feel could have been discussed: Mood change/depression, weight gain/loss, unexpected issues such as constipation, extended healing time and other complications (shoulder, back pain), emotionally coping during recovery. Conclusion: Various themes identified included not only physical aspects but also social consequence of hysterectomy, personal feelings of being "broken" or changed self-image, frustrations, consequences related to sexual intimacy, regrets and depression. Providers should be aware that clearly undergoing hysterectomy is also an emotional experience for most women. (Table Presented).

Obstetrics, Gynecology and Women's Health Services

Talukdar S, **Underwood J**, Atkinson S, and **Sangha R**. Who will suffer from postablation pelvic pain? A retrospective analysis of risk factors *Obstet Gynecol* 2016; 127:141S. PMID: Not assigned. Abstract

S. Talukdar, University of Iowa Hospital, Iowa City, United States

INTRODUCTION: Identifying risk factors for post ablation pain is a critically important task. Data on individual predictors of postablation pain are mixed and conflicting. Our objective was to identify various patient characteristics associated with development of new onset or worsening pelvic pain after endometrial ablation. METHODS: A retrospective cohort study of all patients who underwent endometrial ablation at Henry Ford Health System, during 2012- 2014. Baseline characteristics at the time of ablation, relevant medical comorbidities, and ablation technique and treatment outcome were analyzed. RESULTS: A total of 368 women met the inclusion criteria for the study.

Sixteen percent experienced new or worsening pelvic pain after ablation; 40% of them required a hysterectomy for intractable pain. Only two factors that emerged as potential contributor to postablation pain were history of tubal ligation (adjusted odds ratio [OR] 2.34, 95% confidence interval [CI] 1.21-4.63) and prior pelvic pain (adjusted OR 7.81, 95% CI 2.97-20.98). Age, BMI, prior cesarean sections, endometriosis, preablation dysmenorrhea, presence of uterine fibroid and presumptive diagnosis of adenomyosis were not associated with the development of postablation pain. Ablation technique did not affect the rate of post ablation pain. Patients with postablation pain underwent a hysterectomy within a shorter time than those without pain (P<.001). CONCLUSION: Patient selection for endometrial ablation is crucial. Physicians should counsel women with history of tubal ligation and chronic pelvic pain about the potential for post procedure pain and subsequent treatment failure.

Obstetrics, Gynecology and Women's Health Services

Underwood J, Chiu M, Park H, and Al-Wahab Z. Hair in all the wrong places: Ovarian steroid cell tumor, not otherwise specified: A case series *Obstet Gynecol* 2016; 127:137S-138S. PMID: Not assigned. Abstract

J. Underwood, Henry Ford, Detroit, United States

INTRODUCTION: Ovarian steroid cell tumors, not otherwise specified (NOS), represent 0.1% of all ovarian neoplasm. To our knowledge, cumulative data on steroid cell tumors has not been published. We present a series of four consecutive cases. METHODS: Patients treated for ovarian steroid cell tumor NOS, at three tertiary institutions between 2008 and 2015 were identified by retrospective chart review. Clinical features, tumor characteristics, treatment and outcome were studied. RESULTS: Two patients (age 64, 86) had small 1.8-2.1 cm noninvasive tumors limited to the ovary and two patients (age 48, 57) had large tumors with possible capsular invasion (12 cm) and peritoneal metastasis (15 cm). All four patients had evidence of hirsutism and/or virilization. Three patients had significantly elevated serum testosterone (96-839 ng/dL). No patient exhibited hyperesterogenism. The metastatic tumor had large tumor necrosis, Grade 2-3 nuclear atypia, and strongly positive staining for Immunoperoxidae, Inhibin, and Vimentin. Only the patient with metastatic disease received adjuvant chemotherapy after initial surgery. She is alive after 62 months with recurrent progressive disease. Three patients who did not receive adjuvant treatment remain disease-free after an average follow-up of 35 months. CONCLUSION: Natural history and management of ovarian steroid cell tumor NOS remain unclear. In our small case series, younger age at diagnosis and larger tumor size, but not relative increase in virilization or testosterone level, were observed in possibly invasive and metastatic disease compared to disease compared to non-invasive disease. Collaborative development of a larger case series will increase our understanding of this rare tumor and help establish a management consensus.

Obstetrics, Gynecology and Women's Health Services

Wang W, Kryczek I, Dostal L, Lin H, Tan L, Zhao L, Lu F, Wei S, Maj T, Peng D, He G, Vatan L, Szeliga W, Kuick R, Kotarski J, Tarkowski R, Dou Y, **Rattan R**, **Munkarah A**, Liu JR, and Zou W. Effector t cells abrogate stroma-mediated chemoresistance in ovarian cancer *Cell* 2016; 165(5):1092-1105. PMID: 27133165. Article Request Form

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Effector T cells and fibroblasts are major components in the tumor microenvironment. The means through which these cellular interactions affect chemoresistance is unclear. Here, we show that fibroblasts diminish nuclear accumulation of platinum in ovarian cancer cells, resulting in resistance to platinum-based chemotherapy. We demonstrate that glutathione and cysteine released by fibroblasts contribute to this resistance. CD8(+) T cells abolish the resistance by altering glutathione and cystine metabolism in fibroblasts. CD8(+) T-cell-derived interferon

(IFN)gamma controls fibroblast glutathione and cysteine through upregulation of gamma-glutamyltransferases and transcriptional repression of system xc(-) cystine and glutamate antiporter via the JAK/STAT1 pathway. The presence of stromal fibroblasts and CD8(+) T cells is negatively and positively associated with ovarian cancer patient survival, respectively. Thus, our work uncovers a mode of action for effector T cells: they abrogate stromal-mediated chemoresistance. Capitalizing upon the interplay between chemotherapy and immunotherapy holds high potential for cancer treatment.

Orthopaedics
Frisch NB, **Lynch JR**, **Banglmaier RF**, and **Silverton CD**. The stability of dual-taper modular hip implants: A biomechanical analysis examining the effect of impact location on component stability *Arthroplasty Today* 2016;PMID: Not assigned. Full Text

J.R. Lynch, 3107 Ferris Ave., Royal Oak, MI 48073, USA

Background: The purpose of this study was to investigate the stability of dual-taper modular implants following impaction forces delivered at varying locations as measured by the distraction forces required to disassemble the components. Methods: Distraction of the head-neck and neck-stem (NS) tapers of dual-taper modular implants with 0°, 8°, and 15° neck angles were measured utilizing a custom-made distraction fixture attached to a servohydraulic materials test machine. Distraction was measured after hand pressing the components as well as following a simulated firm hammer blow impaction. Impacts to the 0°, 8°, 15° necks were directed axially in line with the neck, 10° anterior, and 10° proximal to the axis of the neck, respectively. Results: Impaction increased the range of NS component distraction forces when compared to hand pressed components (1125-1743 N vs 248-302 N, respectively). Off-axis impacts resulted in significantly reduced mean (±95% confidence interval) distraction forces (8° neck, 1125 ± 117 N; 15° neck, 1212 ± 73 N), which were up to 35% lower than the mean distraction force for axial impacts to the 0° neck (1743 ± 138 N). Conclusions: Direction of impaction influences stability of the modular interface. The greatest stability was achieved with impaction directed in line with the longitudinal axis of the taper junction. Off-axis impaction of the 8° and 15° neck led to significantly reduced stability at the NS. Improving stability of dual-taper modular hip prostheses with appropriately directed impaction may help to minimize micromotion, component settling, fretting corrosion, and subsequent failure.

Orthopaedics
Liu JZ, **Frisch NB**, Barden RM, Rosenberg AG, **Silverton CD**, and Galante JO. Heterotopic ossification prophylaxis after total hip arthroplasty: Randomized trial of 400 vs 700 cgy *J Arthroplasty* 2016;PMID: 27884418. Full Text

Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan.
Department of Orthopaedic Surgery, Rush University Medical Center, Chicago, Illinois.

BACKGROUND: Heterotopic ossification (HO) is a known complication following total hip arthroplasty. Radiation is an effective prophylaxis, but an optimal protocol has yet to be determined. We performed a randomized, double-blinded clinical trial in high-risk patients to determine the efficacy of 400 vs 700 cGy doses of radiation. METHODS: One hundred forty-seven patients undergoing total hip arthroplasty and at high risk for HO at an urban medical center were randomized to receive either a single 400 or 700 cGy dose of radiation postoperatively. High risk was defined as a diagnosis of diffuse idiopathic skeletal hyperostosis, hypertrophic osteoarthritis, ankylosing spondylitis, or history of previous HO. Radiation was administered on the first or second postoperative day. A single blinded reviewer graded radiographs taken immediately postoperatively and at a minimum of 6 months postoperatively using the Brooker classification. Progression was defined as an increase in Brooker classification. Operative data including surgical approach, implant fixation, revision surgery, and postoperative range of motion data were also collected. RESULTS: A significantly greater portion of patients who received the 400 cGy dose demonstrated progression of HO than patients who received the 700 cGy dose. There were no wound complications. No preoperative factors were associated with a higher rate of progression. Patients who progressed had less flexion on physical examination than patients who did not progress, but this was not clinically significant. CONCLUSION: Seven hundred centigray was superior to 400 cGy in preventing HO formation following total hip arthroplasty in high-risk patients and may be the more effective treatment in this population. Further studies comparing 700 cGy to dosages between 400 and 700 cGy may help to clarify if a more optimal dose can be identified.

Pathology
Calio A, Grignon DJ, Stohr BA, **Williamson SR**, Eble JN, and Cheng L. Renal cell carcinoma with TFE3 translocation and succinate dehydrogenase B mutation *Mod Pathol* 2016;PMID: 27910947. Full Text

Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, IN, USA.
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Translocation renal cell carcinoma and succinate dehydrogenase (SDH)-deficient renal cell carcinoma are now recognized as specific renal tumor types in the World Health Organization (WHO) classification. Both have limited immunohistochemical positivity for epithelial markers, and the spectrum of morphology continues to widen for both of these entities. We identified four renal cell carcinomas with positive TFE3 immunohistochemical staining and negative SDHB staining. The patients (2F, 2M) ranged in age from 19 to 65 years. All tumors were composed, at least in part, of eosinophilic cells. Cytoplasmic inclusions, prominent nucleoli, and mitotic figures were seen in three tumors. Psammoma bodies were also present in two tumors. Using immunohistochemistry, a broad spectrum of commonly used renal tumor markers yielded nonspecific, limited positivity, including uniformly positive reactions for PAX8 but negative results for cathepsin K and HMB45. Fluorescence in situ hybridization results showed the presence of TFE3 gene rearrangement in all four tumors, and molecular analysis revealed SDHB mutations in neoplastic cells of three tumors. In one case, the same SDHB mutation was confirmed in the adjacent non-neoplastic tissue. We report for the first time the presence of both TFE3 translocation and SDHB mutation in the same tumor.Modern Pathology advance online publication, 2 December 2016; doi:10.1038/modpathol.2016.200.

Pathology

Flynt LK, **Veve MP**, **Samuel LP**, and **Tibbets RJ**. Ceftolozane-tazobactam susceptibility testing of Pseudomonas aeruginosa: a comparison of Etest to broth microdilution *J Clin Microbiol* 2016;PMID: 27795348.
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The emergence and spread of multi-drug resistant (MDR) Pseudomonas aeruginosa is a significant burden to healthcare-systems due to poor patient outcomes, serious infection control implications, and limited antibiotic effectiveness.....

Pathology

Kouba E, Simper NB, Chen S, **Williamson SR**, Grignon DJ, Eble JN, MacLennan GT, Montironi R, Lopez-Beltran A, Osunkoya AO, Zhang S, Wang M, Wang L, Tran T, Emerson RE, Baldrige LA, Monn MF, Linos K, and Cheng L. Solitary fibrous tumour of the genitourinary tract: a clinicopathological study of 11 cases and their association with the NAB2-STAT6 fusion gene *J Clin Pathol* 2016;PMID: 27802414. Full Text

Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, Indiana, USA.
Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, Michigan, USA.
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Department of Pathological Anatomy and Histopathology, School of Medicine, Polytechnic University of the Marche Region (Ancona), Ancona, Italy.
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Department of Pathology, Emory University School of Medicine, Atlanta, Georgia, USA.
Michigan Center for Translational Pathology, University of Michigan, Ann Arbor, Michigan, USA.
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AIMS: To characterise clinicopathological features and clinical outcomes of the genitourinary tract solitary fibrous tumours, incorporating NAB2-STAT6 gene fusion status. METHODS: The presence of the molecular hallmark NAB2-STAT6 gene fusion and for the defining fusion partner product STAT6 was assessed in 11 cases of the genitourinary tract solitary fibrous tumours. NAB2-STAT6 gene fusion analysis was performed using a break-apart fluorescence in situ hybridisation (FISH) probe using a probe cocktail with Bacterial artificial chromosome (BAC) clones for STAT6 and NAB2. RESULTS: Eleven solitary fibrous tumours were diagnosed in eight male patients and three female patients with a mean age of 46 years (range: 11-64 years). Four of the tumours had malignant histological features,

and three were considered moderate risk for metastasis. With a mean follow-up time of 61 months, 1 recurred locally and 2 presented at distant metastatic sites. Using a break-apart FISH probe cocktail, we found the NAB2-STAT6 gene fusion and nuclear STAT6 expression in 58% and 91% of cases, respectively. However, the NAB2-STAT6 fusion status was not correlated with STAT6 expression or useful in discriminating between malignant histological features or subsequent clinical outcomes in the genitourinary solitary fibrous tumours. CONCLUSIONS: A subset of solitary fibrous tumours of the genitourinary tract behaved aggressively. Using a break-apart FISH probe cocktail, we found the NAB2-STAT6 gene fusion in 64% of cases. However, the NAB2-STAT6 fusion status was not correlated with STAT6 expression or useful in discriminating between low-risk or high-risk tumours and subsequent clinical outcomes.

Pathology

MacLeod E, Bresler R, Kheradmand T, **Skorupski S**, Gerlach J, and Ho S. Determining the serologic equivalent of a relatively rare common allele DRB1∗11:17 *Hum Immunol* 2016; 77:141. PMID: Not assigned. Abstract

E. MacLeod, Mid-America Transplant, St. Louis, United States

Aim: Many common and well-documented (CWD) alleles have not been assigned official World Health Organization (WHO) approved serologic equivalents, which often makes the reporting of time-sensitive deceased donor typing and virtual crossmatch very challenging. Here we report the characterization of the serologic reactivity of a relatively rare CWD allele, DRB1∗11:17. Methods: A 31 year-old African American female deceased donor was presented for HLA typing using the real-time (RT) PCR and PCR-SSP methods at the low-intermediate resolution. High resolution typing was retrospectively performed by SBT. Serologic specificity was investigated by way of surrogate flow cytometric crossmatch (FCXM) using donor lymphocytes and selected patient sera with well characterized antibody specificities as defined by single antigen solid-phase assays. Results: Donor DR typing was confirmed by all assays as DRB1∗11:01, DRB1∗11:17. According to the NMDP database, DRB1∗11:17 has an overall frequency 0.04% in African Americans, where most commonly found, and accounts for 0.27% of all DR11 alleles reported. While there is no official WHO assigned serologic specificity for DRB1∗11:17, the artificial Neural Network (NN) analysis predicted it to react as DR14. Of the 9 surrogate FCXMs performed using selected sera containing antibody reactivity to DR14 (5 to DRB1∗14:01 only; 2 to DRB1∗14:02 only; 2 to both DRB1∗14:01/14:02) at various strengths (2000-14000 MFI), 8 resulted in positive B-cell crossmatches. No noticeable difference was observed between the reactivity to DRB1∗14:01 vs 14:02. The one negative crossmatch could be attributed to a rather weak DR14 reactivity (<2000 MFI) in that serum. The DR11 reactivity of DRB1∗11:17 could not be determined, as the other donor haplotype also contained a DRB1∗11 allele. Protein sequence analysis indicated that, while DRB1∗11:17 was assigned to the DRB1∗11 allele group, it contained 7 amino acid (aa) substitutions compared to DRB1∗11:01/11:02, whereas it contained 64 aa substitutions as compared to DRB1∗14:01G, indicating a higher sequence homology to DRB1∗14 than to DRB1∗11 alleles. Conclusion: In this study, the serologic specificity of DRB1∗11:17 has been confirmed as DR14, which is consistent to that predicted by the NN analysis.

Pathology

Moonka D, **Nagai S**, **Gadde R**, **Datta L**, **Divine G**, **Abouljoud MS**, and **Salgia R**. Effect of tumor necrosis from loco-regional therapy prior to liver transplantation on hepatocellular carcinoma recurrence after transplant *Hepatology* 2016; 63(1):640A-641A. PMID: Not assigned. Abstract

D. Moonka, Division of Gastroenterology, Henry Ford Hospital, Detroit, United States

Few studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on recurrence of hepatocellular carcinoma (HCC) after LT. We describe results in 181 LT patients. Methods: We evaluated 260 consecutive LT patients with presumed HCC. Patients were excluded for cholangiocarcinoma (9), death within 3 months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients. Patients were evaluated for factors associated with time to HCC recurrence using Kaplan-Meier estimates with log-rank test. Multivariate modeling used Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had 1 treatment, 25 had 2 and 4 had 3 treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium-90 embo-lization. 30 patients had HCC recurrence at a mean of 24.0 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without (P=0.023). A cutoff of 85% necrosis gave a maximal Youden's J statistic for discriminating groups less likely to recur from those more likely. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For 114 patients with < 85% necrosis, 1, 3 and 5

year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant in part because all patients with > 85% necrosis were within Milan. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Pathology

Moonka D, **Shah V**, **Datta L**, **Gadde R**, **Divine G**, **Yoshida A**, **Jafri SM**, and **Salgia R**. Degree of tumor necrosis from pre-transplant loco-regional therapy is associated with tumor free survival after liver transplantation *Transplantation* 2016; 100(7):S429. PMID: Not assigned. Abstract

D. Moonka, Gastroenterology and Hepatology, Henry Ford Health System, Detroit, United States

Introduction: Previous studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on the rate of recurrence of hepatocellular carcinoma (HCC) after transplant. These studies have shown mixed results. We describe our results in 181 LT patients with HCC at our center. Methods: We evaluated 260 consecutive LT patients at our institution with known HCC. Patients were excluded for cholangiocarcinoma (9), death within three months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients of whom 30 had HCC recurrence. Patients were evaluated for a variety of factors for association with time to HCC recurrence using Kaplan-Meier estimates and log-rank tests. Multivariate modeling was done using Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had one treatment, 25 had two and four patients had three treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium (Y-90) embolization. Thirty patients had HCC recurrence at a mean of 24.0 months with a range of 3.4 to 97.6 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without recurrence (P=0.023). A cutoff of 85% tumor necrosis gave the maximal Youden's J statistic for discriminating groups most likely to recur from those less likely to do so. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For the 114 patients with < 85% necrosis, 1, 3 and 5 year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant. Of note, all patients with > 85% necrosis were within Milan criteria on explant. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, the percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Pathology

Sood A, **Williamson SR**, and **Leavitt DA**. Neuroendocrine tumor of the ureter: A zebra among horses *J Endourol Case Rep* 2016; 2(1):204-208. PMID: 27868098. Full Text

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Department of Pathology, Henry Ford Health System , Detroit, Michigan.

Primary neuroendocrine tumors of the upper urinary tract are extremely rare. We report a case of de novo small cell carcinoma of the ureter that presented masquerading as a distal ureteral stone. A 55-year-old lady presented to our clinic with 1 month history of right lower back pain and hematuria. Her history was notable for stage 1B mixed clear cell-endometroid cancer of the uterus status post radical abdominal hysterectomy with adjuvant radiotherapy, 7 years before the current episode. The patient had no evidence of recurrence. Initial noncontrast imaging suggested a 2.5 mm calculus in the distal right ureter and hydronephrosis; however, ureteroscopy revealed a large fleshy mass at the location. Histopathologic evaluation demonstrated the lesion to be primary small cell carcinoma of the ureter, without evidence of it being a derivative of the prior gynecologic malignancy. Metastatic work-up revealed high burden retroperitoneal adenopathy. The patient was started on Cisplatin-based neoadjuvant chemotherapy with plan for

nephroureterectomy in the future. At 3 months follow-up, the patient was doing well with significant shrinkage of retroperitoneal adenopathy and no evidence of disease progression.

Pathology
Williamson SR, Eble JN, and **Palanisamy N**. Sclerosing TFEB rearrangement renal cell carcinoma: A recurring histologic pattern *Hum Pathol* 2016;PMID: 27864122. Full Text

Department of Pathology and Laboratory Medicine, Detroit, MI, USA; Josephine Ford Cancer Institute, Henry Ford Health System, Detroit, MI, USA; Wayne State University School of Medicine, Detroit, MI, USA. Electronic address: seanwill@temple.edu.
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Renal cell carcinoma with TFEB rearrangement [t(6;11)(p21;q13)] was initially recognized to be composed of dual populations of large cells with clear cytoplasm and small cells forming rosettes around hyaline material. With increasing awareness, however, the spectrum of described morphology has been found to be more heterogeneous. We report a 54 year-old woman who underwent partial nephrectomy for a 2.4 cm renal mass, composed of fibrosis, hyalinization, calcification and ossification, and a smaller component of epithelioid cells. Immunohistochemical staining revealed diffuse positivity for cytokeratin AE1/AE3 and PAX8, patchy labeling for melan-A, HMB45, and cathepsin K, and negative caldesmon, SMA, TFE3 protein, carbonic anhydrase IX, CD10, CK7, EMA and inhibin. Fluorescence in situ hybridization confirmed rearrangement of TFEB and not TFE3. Together with one recent case in another report, our findings suggest that extensive sclerosis and ossification may be a less common recurring histology of TFEB rearrangement renal cell carcinoma.

Pathology
Yates SG, Smith S, Tharpe W, Shen YM, and Sarode R. Can an anti-Xa assay for low-molecular-weight heparin be used to assess the presence of rivaroxaban? *Transfus Apher Sci* 2016; 55(2):212-215. PMID: 27377884. Full Text

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BACKGROUND: Due to the convenience afforded by the lack of required laboratory monitoring, direct oral anticoagulants (DOACs) are increasingly used as alternatives to Vitamin-K antagonists for certain medical conditions. However, there are circumstances in which assessment of DOAC plasma concentrations may be helpful in guiding clinical decisions, including patients presenting with either bleeding or thrombosis, or patients requiring urgent invasive procedures. Evaluating the anticoagulant effects of DOACs is often difficult because of the limited availability of DOAC-specific assays in most laboratories. OBJECTIVE: To evaluate the correlation between ex vivo plasma concentrations of rivaroxaban and a chromogenic anti-Xa assay for low-molecular-weight heparin (LMWH) routinely used in our coagulation laboratory. MATERIALS AND METHODS: Twenty-nine blood samples from 20 patients anticoagulated with rivaroxaban (dose; 10-20 mg/day) were evaluated using an anti-Xa assay for LMWH and results were correlated with rivaroxaban plasma concentrations using a rivaroxaban specific assay. RESULTS: A linear dose-dependent relationship was demonstrated between plasma concentrations of rivaroxaban and the chromogenic anti-Xa assay for LMWH (R2 = 0.92). PT and PTT demonstrated poor correlations (R2 = 0.03; and R2 = 0.01, respectively) with rivaroxaban plasma concentrations. CONCLUSION: Findings from this study suggest that if specific assays for rivaroxaban are unavailable, then the chromogenic anti-Xa assay for LMWH may be useful for assessing the anticoagulant effects of rivaroxaban.

Pharmacy
Carreno JJ, Kenney RM, **Divine G**, **Vazquez JA**, and **Davis SL**. Randomized controlled trial to determine the efficacy of early switch from vancomycin to vancomycin alternatives as a strategy to prevent nephrotoxicity in patients with multiple risk factors for adverse renal outcomes (STOP-NT) *Ann Pharmacother* 2016;PMID: 27838680. Full Text

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BACKGROUND: Use of alternative antimicrobials to vancomycin is a potential strategy to reduce acute kidney injury (AKI) in high-risk patients, but current data do not support widespread adoption of this practice. OBJECTIVE: To determine the efficacy of early switch to a nonnephrotoxic alternative for prevention of AKI in high-risk patients who receive vancomycin. METHODS: This was an IRB-approved, prospective randomized controlled trial in a single, tertiary care academic medical center. Patients initially prescribed vancomycin between October 2011 to April 2013 with at least 2 risk factors for AKI were included. Treatment randomization was stratified by indication for therapy. Patients were randomized to continuation of dose-optimized vancomycin or early switch to an alternative antimicrobial agent. The primary end point was nephrotoxicity by consensus guideline definition adjudicated by blinded review; the secondary end point was AKI network-defined AKI. RESULTS: A total of 103 patients were randomized; 100 were included in the modified intent-to-treat population, 51 in the vancomycin group and 49 in the alternative group. The incidence of nephrotoxicity was 6.1% in the alternative therapy arm and 9.8% in the vancomycin group (P = 0.72). The incidence of AKI was 32.7% in the alternative therapy group and 31.4% in the vancomycin group (P = 0.89). CONCLUSIONS: No significant difference in nephrotoxicity or AKI was detected among patients treated with alternative antimicrobials compared with vancomycin. The use of alternative antimicrobial therapy instead of vancomycin solely for the purpose of preventing AKI in high-risk patients does not appear to be warranted.

Pharmacy

Flynt LK, **Veve MP**, **Samuel LP**, and **Tibbets RJ**. Ceftolozane-tazobactam susceptibility testing of Pseudomonas aeruginosa: a comparison of Etest to broth microdilution *J Clin Microbiol* 2016;PMID: 27795348.
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The emergence and spread of multi-drug resistant (MDR) Pseudomonas aeruginosa is a significant burden to healthcare-systems due to poor patient outcomes, serious infection control implications, and limited antibiotic effectiveness.....

Pharmacy

Smith AL, Garwood CL, Bailey T, DeCator D, Elder J, Green A, **Kostoff D**, Lucarotti RL, **MacDonald NC**, Malburg D, Ottney A, Remington TL, and Shuster J. State affiliate initiative to advance ambulatory care practice *Am J Health Syst Pharm* 2016; 73(23):1909-1914. PMID: 27864196. Full Text

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Pharmacy

Venker BT, **Ganti BR**, Lin H, Lee ED, Nunley RM, and Gage BF. Safety and efficacy of new anticoagulants for the prevention of venous thromboembolism after hip and knee arthroplasty: A meta-analysis *J Arthroplasty* 2016;PMID: 27823844. Full Text

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Department of Internal Medicine, Washington University in St. Louis, St. Louis, Missouri; Department of Pharmacy Services, Henry Ford Hospital, Detroit, Michigan.
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Department of Internal Medicine, Washington University in St. Louis, St. Louis, Missouri; Carolina Rehabilitation and Surgical Associates, Raleigh, North Carolina.
Department of Internal Medicine, Washington University in St. Louis, St. Louis, Missouri; Department of Orthopedic Surgery, Washington University in St. Louis, St. Louis, Missouri.
Department of Internal Medicine, Washington University in St. Louis, St. Louis, Missouri.

BACKGROUND: Venous thromboembolism (VTE) is a common and potentially fatal complication of arthroplasty. METHODS: We reviewed randomized trials to determine which anticoagulant has the best safety and efficacy in hip and knee arthroplasty patients. We searched PubMed, MEDLINE, and EMBASE through January 2016. RESULTS: Compared to enoxaparin (most commonly dosed 40 mg once daily), the relative risk (RR) of VTE was lowest for edoxaban 30 mg once daily (0.49; 95% confidence interval [CI], 0.32-0.75), fondaparinux 2.5 mg once daily (0.53; 95% CI, 0.45-0.63), and rivaroxaban 10 mg once daily (0.55; 95% CI, 0.46-0.66), and highest for dabigatran 150 mg once daily (1.19; 95% CI; 0.98-1.44). The RR of major/clinically relevant bleeding was lowest for apixaban 2.5 mg twice daily (0.84; 95% CI; 0.70-0.99) and highest for rivaroxaban (1.27; 95% CI, 1.01-1.59) and fondaparinux (1.64; 95% CI, 0.24-11.35). Fondaparinux was the only agent that was more effective than enoxaparin 30 mg twice daily (VTE RR = 0.58; 95% CI, 0.43-0.76). CONCLUSION: With the possible exception of apixaban, newer anticoagulants that lower the risk of postoperative VTE increase bleeding.

Pharmacy

Zasowski EJ, Trinh TD, Claeys KC, Casapao AM, Sabagha N, Lagnf AM, Klinker KP, **Davis SL**, and Rybak MJ. A multicenter observational study of ceftaroline fosamil for methicillin-resistant staphylococcus aureus bloodstream infections *Antimicrob Agents Chemother* 2016;PMID: 27895012. Full Text

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Novel therapies for methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infection (BSI) are needed in the setting of reduced antibiotic susceptibilities and therapeutic failure. Ceftaroline is an advanced generation cephalosporin with MRSA activity. Although not FDA approved for MRSA BSI, ceftaroline has generated much interest as a potential treatment option. However, detailed description of its use in this setting remains limited. To address this, we conducted a retrospective, multicenter, observational study of adult patients with MRSA BSI treated with at least 72 hours of ceftaroline from 2011 to 2015. Safety outcomes were examined in the overall cohort while efficacy outcomes were examined among patients who had not cleared their BSI prior to ceftaroline initiation. Data were also stratified by ceftaroline monotherapy or combination therapy. Predictors of clinical failure on ceftaroline were also sought. Overall, 211 patients were included in the safety population; Clostridium difficile infection, rash, and neutropenia occurred in 6 (2.8%), 7 (3.3%), and 3 (1.4%) of patients, respectively. Clinical success was observed in 86 (68.3%) of the 126 patients included in efficacy population. The monotherapy and combination therapy subgroups had a similar proportion of patients experiencing success (69.7 and 64.9%, respectively). The median BSI duration post-ceftaroline was 2 (1 - 4) days among monotherapy and 3 (1.5 - 5) days for combination therapy. Higher APACHE II score and comorbid malignancy independently predicted treatment failure. Ceftaroline appears effective for MRSA BSI as both monotherapy and combination therapy. However, comparative studies are needed to further delineate the role of ceftaroline in MRSA BSI treatment.

Prevention and Community Health
Keteyian CK, Runge MS, Reddy SG, and Nallamothu BK. Talking trash *Bmj* 2016; 355:i5996. PMID: 27856409. Full Text

Prevention and Community Health and Jackson Health Network, Henry Ford Allegiance Health, 205 N East Avenue, Jackson, MI 49201, USA courtland.keteyian@allegiancehealth.org.
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Public Health Sciences
Bazzi M, **Abdullah N**, **Karabon P**, Chick J, and **Dabaja AA**. Trends in embryo transfer rate, multiple birth rate, and pregnancy rate in response to the american society of reproductive medicine's recommendation to limit embryotransfer *Fertility and Sterility* 2016; 106:e325. PMID: Not assigned. Abstract

M. Bazzi, Wayne State University, School of Medicine, Dearborn, United States

OBJECTIVE: Multiple embryo transfer during in vitro fertilization (IVF) can lead to higher order pregnancy, and can complicate fetal and maternal health. The American Society for Reproductive Medicine (ASRM) passed recommendation in 1977 to reduce the number of embryos transferred during IVF. We evaluated the long-term impact of ASRM's recommendation on embryo transfer rate (ETR), multiple birth rate (MBR), and pregnancy rate (PR) from 1997 to 2012. DESIGN: Retrospective analysis of previously published ETR. MATERIALS AND METHODS: Using publicly available data from the Centers for Disease Control and Prevention (CDC), we calculated the national ETR, MBR, and PR for a given year. The fertility success reports provided data stratified by the following age groups: less than 35 years old, between 35 and 40 years old and greater than 40 years old. For statistical analysis, we used a multilevel linear mixed effects model to assess temporal/ time trends. Temporal trends were tested using the Estimated Annual Percentage Change (EAPC) methodology. All statistical analysis was performed using SAS 9.4 (Cary, North Carolina; SAS Institute). RESULTS: Analyses from our study showed that the estimated annual percent change in embryo transfer rate and multiple birth rate is -3.36% and -1.90%, respectively (p-value <0.01) from 1997 to 2012. The pregnancy rate has improved between 1997 and 2012 with an estimated average percent change of 1.90% (p-value <0.01). CONCLUSIONS: Professional societies' recommendation to reduce the number of embryos transferred has effectively reduced national embryo transfer rate without compromising pregnancy rates.

Public Health Sciences
Carreno JJ, Kenney RM, **Divine G**, **Vazquez JA**, and **Davis SL**. Randomized controlled trial to determine the efficacy of early switch from vancomycin to vancomycin alternatives as a strategy to prevent nephrotoxicity in patients with multiple risk factors for adverse renal outcomes (STOP-NT) *Ann Pharmacother* 2016;PMID: 27838680. Full Text

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BACKGROUND: Use of alternative antimicrobials to vancomycin is a potential strategy to reduce acute kidney injury (AKI) in high-risk patients, but current data do not support widespread adoption of this practice. OBJECTIVE: To determine the efficacy of early switch to a nonnephrotoxic alternative for prevention of AKI in high-risk patients who receive vancomycin. METHODS: This was an IRB-approved, prospective randomized controlled trial in a single, tertiary care academic medical center. Patients initially prescribed vancomycin between October 2011 to April 2013 with at least 2 risk factors for AKI were included. Treatment randomization was stratified by indication for therapy. Patients were randomized to continuation of dose-optimized vancomycin or early switch to an alternative antimicrobial agent. The primary end point was nephrotoxicity by consensus guideline definition adjudicated by blinded review; the secondary end point was AKI network-defined AKI. RESULTS: A total of 103 patients were randomized; 100 were included in the modified intent-to-treat population, 51 in the vancomycin group and 49 in the alternative group. The incidence of nephrotoxicity was 6.1% in the alternative therapy arm and 9.8% in the vancomycin group (P = 0.72). The incidence of AKI was 32.7% in the alternative therapy group and 31.4% in the

vancomycin group (P = 0.89). CONCLUSIONS: No significant difference in nephrotoxicity or AKI was detected among patients treated with alternative antimicrobials compared with vancomycin. The use of alternative antimicrobial therapy instead of vancomycin solely for the purpose of preventing AKI in high-risk patients does not appear to be warranted.

Public Health Sciences
Henein F, **Prabhakar D**, **Peterson EL**, **Williams LK**, and **Ahmedani BK**. A prospective study of antidepressant adherence and suicidal ideation among adults *Prim Care Companion CNS Disord* 2016; 18(6)PMID: 27907275.
Article Request Form

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Public Health Sciences
Isrow D, **Burmeister C**, **Hanna RK**, and **Elshaikh MA**. Survival endpoints for young women with early stage uterine endometrioid carcinoma: a matched analysis *Eur J Obstet Gynecol Reprod Biol* 2016; 207:115-120. PMID: 27838535. Full Text

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OBJECTIVES: Younger age is thought to be a favorable prognostic factor in women with endometrial carcinoma (EC). Survival endpoints were compared between two matched groups of patients with early stage EC: women 45 years or younger and women older than 45 years. METHODS AND MATERIALS: Two matched groups of patients were created based on stage, grade, lymph node dissection and adjuvant management. Recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) were calculated. RESULTS: A total of 525 patients (88 younger patients and 437 older patients, matched 1:5) were included in this study. The two groups were well balanced except for less myometrial invasion in the younger patients. There were no significant differences between younger and older patients in regards to 5-year RFS (94% vs. 91%, p=0.6902). Similarly, there was no significant difference in regards to DSS (96% vs. 97%, p=0.9000). While 5-year OS was similar for both groups (89% vs. 89%, p=0.9942), 10-year OS was longer in the younger group (83% vs. 68% with p=0.13). On multivariate analysis for RFS, the presence of lymphovascular space invasion was the only predictor of shorter RFS (p=0.0007). Tumor grade (p=0.0002) and lower uterine segment involvement (p=0.0141) were independent predictors of shorter DSS. Older age (p<0.001) and stage II (p=0.01) were the only predictors of shorter OS. CONCLUSIONS: When matched based on tumor stage, grade and adjuvant management, our study suggests that there is no difference in survival endpoints between younger and older patients with early stage endometrial carcinoma.

Public Health Sciences
Li J, **Gordon SC**, **Rupp LB**, **Zhang T**, **Trudeau S**, Holmberg SD, Moorman AC, Spradling PR, Teshale EH, Boscarino JA, Daida YG, Schmidt MA, and **Lu M**. Long-term progression of viral load and serum markers of fibrosis among treated and untreated patients with chronic hepatitis B *J Gastroenterol Hepatol* 2016;PMID: 27888529.
Full Text

Department of Public Health Sciences, Henry Ford Health System, Detroit, MI, USA.
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BACKGROUND AND AIMS: Antiviral therapy for patients with hepatitis B (HBV) infection is generally deferred for "immune inactive" patients, although longitudinal changes in viral load and liver fibrosis remain understudied in this population. Likewise, in treated patients, the temporal relationship between changes in viral load and liver fibrosis is not well-characterized. Using data from the Chronic Hepatitis Cohort Study, we investigated viral load and the Fibrosis-4 index (FIB4, a serum-based marker of liver fibrosis) trajectories in both untreated and treated HBV patients. MATERIALS AND METHODS: We applied a bivariate, piecewise, linear spline, mixed-effects modeling approach to data from 766 HBV patients (342 untreated, 424 treated). Treatment selection bias was adjusted using propensity scores. Multiple sensitivity analyses were used to confirm results in untreated patients. RESULTS: Among all untreated patients, FIB4 began to increase by 0.9% per month (11% per year) ($p < 0.05$) at 28 months post-index date, suggesting fibrosis progression. Significant FIB4 progression was also observed within a subgroup analysis of "immune inactive" untreated patients. In treated patients, viral load declined 31.8% per month ($p < 0.05$) for the first 5 months after treatment initiation, and 1.4-1.7% per month ($p < 0.05$) thereafter. At 5 months after treatment initiation, FIB4 began to decline 0.5% per month ($p < 0.05$), stabilizing at 28 months. CONCLUSION: Among untreated HBV patients, FIB4 gradually increases over time, suggesting fibrosis progression, even in those patients designated as immune inactive. In treated patients, antiviral therapy results in a rapid decline in viral load followed by a delayed decline in markers of liver fibrosis.

Public Health Sciences

Lu M, **Gordon SC**, **Li J**, **Rupp LB**, **Zhou Y**, Moorman AC, Spradling P, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, **Trudeau S**, and Holmberg SD. Hepatitis C complications: Prevalence and disparities in a large US cohort 2006-2014 *Hepatology* 2016; 63(1):95A-96A. PMID: Not assigned. Abstract

M. Lu, Public Health Science, Henry Ford Health System, Detroit, United States

The burden of hepatitis C virus (HCV)-related cirrhosis, decompensated cirrhosis, and mortality has not been well-described in a large “real world” US population. We investigated trends in the prevalence of cirrhosis and decompensated cirrhosis, and incidence of mortality, among HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS) from 2006-2014. Methods: CHeCS is a longitudinal observational study of hepatitis patients from 4 large US health systems. Cirrhosis was ascertained using ICD9 codes, liver biopsy reports, and serum markers of fibrosis. Decompensated cirrhosis was ascertained using a set of ICD9 codes that have been validated as predictive of decompensated cirrhosis. We used join-point modeling (univariate and multivariate) to identify rates of change in prevalence over time as well as “break points” that indicate different phases of Annual Percentage Change (APC). Results: Of 11,286 adult HCV-infected patients, prevalence of cirrhosis increased from 10% in 2006 to 28% in 2014. Join-point analysis identified a breakpoint at 2007, with adjusted APCs of 49.1 (2006-2007; $p<0.05$) and 9.5 (2007-2014; $p<0.05$). Prevalence of decompensated cirrhosis increased from 3% in 2006 to 7% in 2014, with two breakpoints (at 2008 and 2012) and three segments, with APCs of 25.9 (2006-2008; $p<0.05$), 8.7 (2008-2012; $p<0.05$), and 1.4 (2012-2014). Incidence of all-cause mortality increased from 1.1% in 2006 to 3.1% in 2013, with a breakpoint in 2010 and APCs of 20.0 (2006-2010; $p<0.05$) and 4.2 (2010-2013). Older patients, Asian/Pacific Islanders, and men all demonstrated higher prevalence of cirrhosis and decompensated cirrhosis. Black patients demonstrated the highest incidence of all-cause mortality. Conclusions: Over the past decade, prevalence of cirrhosis among HCV patients in this US cohort increased almost 3-fold. During the same time period, prevalence of decompensated cirrhosis and incidence of all-cause mortality more than doubled, although the increase in both plateaued in recent years (Figure Presented).

Public Health Sciences

Lu M, **Li J**, **Rupp LB**, Boscarino JA, Raebel M, Schmidt MA, Haller IV, Daida Y, Rodriguez CV, Sahota A, VanWormer JJ, Romanelli RG, Vincent J, and **Gordon SC**. Prevalence of primary biliary cholangitis (PBC) in large US health care systems: Case ascertainment using electronic health records *Hepatology* 2016; 63(1):196A. PMID: Not assigned. Abstract

M. Lu, Public Health Science, Henry Ford Health System, Detroit, United States

There is little data on the prevalence of primary biliary cholangitis (PBC) in the US. Estimates of prevalence vary widely- from 1.91 to 40.2 per 100,000 persons-depending on the rigor of the method used. We developed a method to ascertain PBC cases using electronic health record (EHR) data and report PBC prevalence among patients receiving care at one of 11 US health systems associated with the Fibrotic Liver Disease (FOLD) Consortium. Methods: We used broad initial EHR inclusion criteria (positive/abnormal anti-mitochondrial antibody test [AMA]; ICD-9 diagnosis code for PBC [571.6]; or receipt of the drug ursodeoxycholic acid) to ensure capture of all possible PBC cases. Chart review was conducted to confirm PBC in a random sample of patients, stratified by likelihood of PBC and year of diagnosis. Next, a Classification and Regression Tree (CART) model, starting with 15 EHR-based

variables, was developed using a learning sample. The optimized PBC CART model was validated using 20-fold cross-validation. Overall prevalence was estimated using CART-identified PBC patients as the numerator, and number of patients receiving care (defined as either ≥1 or ≥2 encounters with participating health systems from 2003-2014) as the denominator. Results: Among 1.4 million patients seen at FOLD health systems between 2003 and 2014, 3711 met at least one initial inclusion criterion; 421 of these were selected for chart review. A CART model with five variables (AMA positive, PBC ICD-9 diagnosis code, alkaline phosphatase >120 IU/L, sex, and age) achieved optimal classification (area under the receiver operator characteristic curve: 0.94 for the learning sample; 0.90 using 20-fold cross-validation). Validation results had specificity=0.90; sensitivity= 0.90; positive predictive value (PPV)=0.83; and negative predictive value (NPV)=0.94. In a subset of 183 recent patients who met one of the initial inclusion criteria during 2010-2014, results showed specificity=0.95; sensitivity=0.82; PPV=0.85; and NPV=0.94. Application of the CART algorithm to all 3711 patients who met at least one initial inclusion criteria identified 589 PBC patients. Twelve-year period prevalence was 41.8 or 41.6 per 100,000, based on either ≥1 or ≥2 heath system encounters. The ratio of women to men was 9:2. Conclusions: An algorithm applied to EHR data can efficiently and accurately identify patients with PBC. Chart review at the ten remaining FOLD sites will be used to validate the algorithm; PBC prevalence will then be determined across the Consortium. Given the rarity of PBC, leveraging automated EHR-based identification could facilitate research into this serious autoimmune condition.

Public Health Sciences

Moonka D, **Nagai S**, **Divine G**, and **Salgia R**. Influence of donor age and cold ischemia on recurrence of hepatocellular carcinoma after liver transplantation *Transplantation* 2016; 100(7):S427. PMID: Not assigned. Abstract

D. Moonka, Gastroenterology and Hepatology, Henry Ford Health System, Detroit, United States

Introduction: The role of donor age on recurrence of hepatocellular carcinoma (HCC) after liver transplant (LT) is not clear. In the current analysis, we evaluate the impact of donor age and cold ischemia time on HCC recurrence after LT. Methods: We evaluated 303 consecutive LT patients at our institution with HCC. Nine were excluded because of findings of cholangiocarcinoma, 11 were excluded because of death within three months and one because of positive HCC margins at LT leaving 282 patients. . Patients were evaluated for a variety of factors for association with time to HCC recurrence using Kaplan-Meier estimates and logrank tests. Multivariate modeling was done using Cox regression analysis. Results and Discussion: In the 282 patients, there were 41 HCC recurrences (14.5%) occurring at a median of 17 months and a mean of 22.2 months and a range of 22 to 98 months. On univariate analysis, factors associated with HCC recurrence were cold ischemia (P < 0.001), donor age (P=0.025), tumor burden within Milan criteria on explant (P < 0.001), maximum alpha-fetoprotein (AFP) (P=0.005) and AFP at time of LT (P < 0.001), poorly differentiated histology (P < 0.001), vascular invasion (P < 0.001) and percent necrosis (P=0.017) in those undergoing pre-LT treatment. Patients with HCC recurrence had a donor age of 47.0 ± 16.7 and those without had a donor age of 41.2 ± 16.2 (P=0.038). Patients with recurrence had a cold ischemia time in hours of 6.8 ± 2.1 vs 5.6 ± 1.7 in those without (P=0.001). For both donor age and cold ischemia, the Youden's J statistic was used to determine an optimal cutoff to discriminate between patients with and without recurrence. The 209 patients with donors less than 55 years old had 1, 3 and 5 year tumor free survival of 93.7%, 90.2% and 87.3% vs 91.5%, 78.4% and 70.3% in the 73 patients with donors over 55 (P=0.009). The 119 patients with cold ischemia less than 5.5 hours had 1, 3 and 5 year tumor free survival of 95.8%, 92.6% and 91.0% vs 91.2%, 82.7% and 76.6% in the 150 patients over 5.5 hours (P=0.006). The 37 patients with donors over 55 and cold ischemia over 5.5 hours had 1, 3 and 5 year tumor free survival of 88.7%, 67.0% and 57.4% vs 95.4%, 92.5%, and 92.5% for the 88 patients with both lower donor age and shorter cold ischemia. In a multivariate analysis controlling for tumor burden, histology and vascular invasion: donor age (P=0.007), cold ischemia (P=0.005), Milan criteria on explant (P=0.002), maximum AFP (P=0.016), AFP at OLT (P=0.004), poorly differentiated histology (P < 0.001) and vascular invasion (P=0.002) were associated with time to tumor recurrence Conclusions: Both lower donor age and shorter cold ischemia time were independently associated with improved tumor free survival after liver transplant. If confirmed in larger cohorts, these represent potentially modifiable factors in liver transplant patients with liver cancer.

Public Health Sciences

Moonka D, **Nagai S**, **Gadde R**, **Datta L**, **Divine G**, **Abouljoud MS**, and **Salgia R**. Effect of tumor necrosis from loco-regional therapy prior to liver transplantation on hepatocellular carcinoma recurrence after transplant *Hepatology* 2016; 63(1):640A-641A. PMID: Not assigned. Abstract

D. Moonka, Division of Gastroenterology, Henry Ford Hospital, Detroit, United States

Few studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on recurrence of hepatocellular carcinoma (HCC) after LT. We describe results in 181 LT patients. Methods: We evaluated 260 consecutive LT patients with presumed HCC. Patients were excluded for cholangiocarcinoma (9),

death within 3 months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients. Patients were evaluated for factors associated with time to HCC recurrence using Kaplan-Meier estimates with log-rank test. Multivariate modeling used Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had 1 treatment, 25 had 2 and 4 had 3 treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium-90 embo-lization. 30 patients had HCC recurrence at a mean of 24.0 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without (P=0.023). A cutoff of 85% necrosis gave a maximal Youden's J statistic for discriminating groups less likely to recur from those more likely. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For 114 patients with < 85% necrosis, 1, 3 and 5 year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant in part because all patients with > 85% necrosis were within Milan. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Public Health Sciences

Moonka D, **Shah V**, **Datta L**, **Gadde R**, **Divine G**, **Yoshida A**, **Jafri SM**, and **Salgia R**. Degree of tumor necrosis from pre-transplant loco-regional therapy is associated with tumor free survival after liver transplantation *Transplantation* 2016; 100(7):S429. PMID: Not assigned. Abstract

D. Moonka, Gastroenterology and Hepatology, Henry Ford Health System, Detroit, United States

Introduction: Previous studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on the rate of recurrence of hepatocellular carcinoma (HCC) after transplant. These studies have shown mixed results. We describe our results in 181 LT patients with HCC at our center. Methods: We evaluated 260 consecutive LT patients at our institution with known HCC. Patients were excluded for cholangiocarcinoma (9), death within three months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients of whom 30 had HCC recurrence. Patients were evaluated for a variety of factors for association with time to HCC recurrence using Kaplan-Meier estimates and log-rank tests. Multivariate modeling was done using Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had one treatment, 25 had two and four patients had three treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium (Y-90) embolization. Thirty patients had HCC recurrence at a mean of 24.0 months with a range of 3.4 to 97.6 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without recurrence (P=0.023). A cutoff of 85% tumor necrosis gave the maximal Youden's J statistic for discriminating groups most likely to recur from those less likely to do so. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For the 114 patients with < 85% necrosis, 1, 3 and 5 year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant. Of note, all patients with > 85% necrosis were within Milan criteria on explant. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, the percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Public Health Sciences

Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, and Holmberg SD. Uptake of and factors associated with direct-acting antiviral therapy among patients infected with

hepatitis C virus in the chronic hepatitis cohort study, 2014-2015 *Hepatology* 2016; 63(1):10A-11A. PMID: Not assigned. Abstract

P.R. Spradling, Division of Viral Hepatitis, CDC, Atlanta, United States

Background: Limited information is available describing the uptake of direct acting antiviral (DAA) therapy for hepatitis C virus (HCV) infection among patients in general US healthcare settings. Methods: We analyzed data collected from HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS), an observational cohort study involving patients from healthcare organizations in Michigan, Pennsylvania, Oregon, and Hawaii, limiting analysis to patients with a clinical encounter during the previous two years. Uptake was defined as the proportion of patients infected with HCV as of December 31, 2013 who were prescribed a DAA regimen (with or without interferon) during 2014 and started the regimen by August 31, 2015. Using multivariable analysis and controlling for relevant variables, we examined demographic and clinical characteristics associated with receipt of DAAs. Results: The cohort was comprised of 10,293 HCV-infected patients as of December 31, 2013, of whom 544 (5.3%) started a DAA regimen by August 31, 2015. Factors independently associated with receipt of DAAs included higher annual income (adjusted Odds Ratios [aOR] 2.4 and 1.7 for income >$50K and $30K-$50K, respectively, vs. <$30K), higher FIB4 score (aORs 2.1, 2.0, and 1.5 for FIB4 >5.88, 3.25-5.88, 2.0-<3.25, respectively, vs. <2.0), genotype 2 infection (aOR 2.2, vs. genotype 1), higher Charlson comorbidity score (aORs 1.3 and 1.4 for scores ≥2 and 1, respectively, vs. score of 0), pre-2014 treatment failure (aOR 1.9, vs. treatment-naive), and HIV coin fection (aOR 1.9, vs. HCV monoinfection). Factors associated with a reduced likelihood of DAA receipt included non-Hispanic Black race/ethnicity (aOR 0.7, vs. non-Hispanic Whites), having Medicaid coverage (aOR 0.5, vs. private insurance), and receipt of care at one of the study sites (aOR 0.3, vs. a tertiary hepatology referral site). Sex, age, and duration of follow- up were not associated with receipt of DAAs. Conclusions: Among patients in these general US healthcare settings, uptake of DAA therapy was low from January 2014-August 2015, and especially so among minority and Medicaid patients. Targeted efforts to improve access to DAAs for these patients are essential to reduce morbidity and mortality from HCV infection.

Public Health Sciences

Spradling PR, Xing J, **Rupp LB**, Moorman AC, **Gordon SC**, **Lu M**, Teshale EH, Boscarino JA, Daida Y, Schmidt MA, and Holmberg SD. Preliminary clinical outcome data among patients with hepatitis C virus infection receiving direct-acting antiviral therapy in the Chronic Hepatitis Cohort Study, 2014-2015 *Hepatology* 2016; 63(1):487A-488A. PMID: Not assigned. Abstract

P.R. Spradling, Division of Viral Hepatitis, CDC, Atlanta, United States

Background: Data describing clinical outcomes of direct-acting antiviral (DAA) therapy among patients infected with hepatitis C virus (HCV) in general healthcare settings are limited. We examined DAA-associated outcomes among HCV-infected patients in the Chronic Hepatitis Cohort Study (CHeCS), an observational study conducted at 4 US healthcare organizations. Methods: Patients who began a DAA regimen from January 2014-August 2015 were included in the analysis. We examined frequency of treatment completion and of sustained viral response (SVR) 12 weeks post-treatment vs. no SVR by sociodemographic, clinical, and treatment-related factors, and conducted multivariable analysis to identify factors independently associated with SVR. Results: Of 613 patients who began an initial DAA regimen during the study period, 212 (48%) were treatment experienced, 210 (54%) had cirrhosis, 81 (18%) were of black race, and 24 (5%) were HIV-coinfected: 280 (46%) had HCV genotype 1a (G1a); 136 (22%) had G1b; 107 (17%) had G2; 68 (11%) had G3; 5 (1%) had G4-6; and 17 (3%) had mixed genotype infection. Overall, 401 (65%) patients received a sofosbuvir (SOF) regimen without ledipasvir (LDV) (i.e., SOF ± simeprevir or daclatasvir ± ribavirin [RBV]) and 211 (34%) received SOF with LDV ± RBV. No patients received an ombitasvir-containing regimen. Of 545 (89% of 613) patients with available SVR data, 463 (85%) achieved SVR. Among patients with G1a, frequencies of SVR ranged from 77% (SOF without LDV and no RBV) to 96% (SOF with LDV ± RBV); among those with G1b, 70% (SOF regimen without LDV + RBV) to 98% (SOF with LDV ± RBV). The frequency of SVR was 83%, 80% and 75% among patients with G2, G3, and G4-6 infection, respectively. In multivariable analysis controlling for all variables, the sole factor independently associated with SVR was receipt of SOF with LDV ± RBV (aOR 6.1 vs. SOF regimen without LDV and no RBV). Neither age, sex, race/ethnicity, previous treatment status, presence of cirrhosis, genotype, comorbidity score, body mass index, or HIV coinfection were associated with SVR. Of the 613 patients who initiated treatment, 68 (11%) either had completed treatment but did not yet have SVR data available (n=32), were still receiving treatment at the close of the study period (n=22), or stopped treatment early (n=14). Conclusions: Among patients who received DAAs in these general healthcare settings, half of whom had cirrhosis and previous treatment, the frequency of treatment completion and SVR was high. Receipt of a regimen other than SOF with LDV was associated with a lower likelihood of achieving SVR.

Public Health Sciences

Teshale EH, Zhong Y, Moorman AC, Spradling PR, Holmberg SD, **Rupp LB**, **Lu M**, **Gordon SC**, Boscarino JA, Daida Y, and Schmidt MA. Alcohol use disorder among chronic hepatitis C patients: Prevalence and treatment outcome, CHeCS, 2006-2013 *Hepatology* 2016; 63(1):873A-874A. PMID: Not assigned. Abstract

E.H. Teshale, CDC, Atlanta, United States

Background: Alcohol use in patients with chronic hepatitis C (CHC) results in progression of liver disease and represents a barrier to antiviral therapy. We sought to determine the prevalence of alcohol abuse and alcohol-related liver disease among CHC patients to assess their access to HCV treatment. Methods: We used CHeCS data collected from CHC patients seen in four large U.S. healthcare systems from 2006-2013. Among patients with documented ICD 9 codes indicative of any alcohol use disorder defined as alcohol abuse/dependence and alcohol-related liver disease, we determined the percentage of patients with any alcohol disorder, with alcohol abuse/dependence, and with alcohol-related liver disease who received HCV treatment. We used multivariable analysis to identify factors associated with HCV treatment by alcohol status. Results: Of the 11,636 CHC patients, 3,553 (30.5%) had at least one documented ICD-9 code indicative of any alcohol use disorder. Among those with any alcohol use disorder, 70.4% were male, 92.5% were aged >44 years, 58.7% were white, and 19.9% had alcohol-related liver disease. Overall, 40.3% of CHC patients received HCV treatment. Only 30.4% of those with alcohol abuse and 50.4% of those with alcohol-related liver disease received treatment. Sustained virologic response rates were 41.6% overall, 44.7% for those with alcohol abuse, and 28.4% for those with alcohol-related liver disease. In univariate analysis HCV treatment was associated with age, race, household income, ever having biopsy and biopsy stage ($p<0.01$). Controlling for age, gender, race, and household income, persons with alcohol abuse were less likely [adjusted odds ratio (aOR) = 0.54 (0.48-0.61)] and those with alcohol- related liver disease were more likely [aOR =1.38 (1.18- 1.63)] to receive HCV treatment than those with no alcohol use disorder. Conclusion: Approximately one third of CHC patients had a recorded diagnosis, indicative of an alcohol use disorder. Although patients diagnosed with alcohol-related liver disease were more likely to receive HCV treatment than those with an alcohol abuse diagnosis, treatment and the response to treatment for patients with either diagnosis were suboptimal overall. Effective direct acting antiviral treatment with greater tolerability and of shorter duration may improve the likelihood of treatment and treatment outcome among all patients, including those with an alcohol use disorder.

Pulmonary

Ouellette DR, Patel S, Girard TD, Morris PE, Schmidt GA, Truwit JD, Al-Hazzani W, Burns SM, Epstein SK, Esteban A, Fan E, Ferrer M, Fraser GL, Gong M, Hough CL, Mehta S, Nanchal R, Pawlik AJ, Schweickert W, Sessler CN, Strom T, and Kress JP. Liberation from mechanical ventilation: An official american college of chest physicians/american thoracic society clinical practice guideline: Inspiratory pressure augmentation during spontaneous breathing trials, protocols minimizing sedation, and non-invasive ventilation immediately after extubation *Chest* 2016;PMID: 27818331. Full Text

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BACKGROUND: An update of evidence-based guidelines concerning liberation from mechanical ventilation is needed as new evidence has become available. The American College of Chest Physicians (CHEST) and the American Thoracic Society (ATS) have collaborated to provide recommendations to clinicians concerning ventilator liberation. METHODS: Comprehensive evidence syntheses, including meta-analyses, were performed to summarize all available evidence relevant to the guideline panel's questions. The evidence was appraised using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach and the results were summarized in evidence profiles. The evidence syntheses were discussed and recommendations developed and approved by a multi-disciplinary committee of experts in mechanical ventilation. RESULTS: Recommendations for three PICO (population, intervention, comparator, outcome) questions concerning ventilator liberation are presented in this document. The guideline panel considered the balance of desirable (benefits) and undesirable consequences (burdens, adverse effects, costs), quality of evidence, feasibility, and acceptability of various interventions with respect to the selected questions. Conditional (weak) recommendations were made to use inspiratory pressure augmentation in the initial spontaneous breathing trial (SBT), and to use protocols to minimize sedation, for patients ventilated for more than 24 hours. A strong recommendation was made to use preventative non-invasive ventilation (NIV) for high-risk patients ventilated for more than 24 hours immediately after extubation to improve selected outcomes. The recommendations were limited by the quality of the available evidence. CONCLUSION: The guideline panel provided recommendations for inspiratory pressure augmentation during an initial SBT, protocols minimizing sedation, and preventative NIV, in relation to ventilator liberation.

Radiation Oncology

Berman AT, Rosenthal SA, Moghanaki D, Woodhouse KD, **Movsas B**, and Vapiwala N. Focusing on the "person" in personalized medicine: The future of patient-centered care in radiation oncology *J Am Coll Radiol* 2016; 13(12 Pt B):1571-1578. PMID: 27888944. Full Text

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Numerous efforts in radiation oncology aim to improve the value of clinical care. To evaluate the success of these efforts, outcome measures must be well defined and incorporate the beliefs of the patients they affect. These outcomes have historically centered on rates of tumor control, overall survival, and adverse events as perceived and reported by providers. However, the future of patient-centered care in radiation oncology is increasingly focusing on the "person" in the population and the individual in the studies to more closely reflect the ideals of personalized medicine. Formally known as patient-centered outcomes, this metric encompasses parameters of patient satisfaction, engagement, and treatment compliance. Evaluations that investigate the safety and efficacy of treatments are increasingly soliciting participation from patients within a model of shared decision making that improves patients' knowledge, satisfaction, physical and emotional well-being, and trust in providers. Modern clinical trials that embrace this approach may even focus on patient-reported outcomes as the primary end point, as opposed to time-honored physician-reported events. The authors explore the growing role of patient-centered care, the incorporation of shared decision making, and the relevant body of existing and developing literature on this topic in radiation oncology. The authors report recent discoveries from this area of study and describe how they can not only support high-quality, high-value patient care but also enhance recruitment to clinical oncology trials, both of which are challenging to achieve in today's relatively resource-strapped environment.

Radiation Oncology

Isrow D, **Burmeister C**, **Hanna RK**, and **Elshaikh MA**. Survival endpoints for young women with early stage uterine endometrioid carcinoma: a matched analysis *Eur J Obstet Gynecol Reprod Biol* 2016; 207:115-120. PMID: 27838535. Full Text

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OBJECTIVES: Younger age is thought to be a favorable prognostic factor in women with endometrial carcinoma (EC). Survival endpoints were compared between two matched groups of patients with early stage EC: women 45 years or younger and women older than 45 years. METHODS AND MATERIALS: Two matched groups of patients were created based on stage, grade, lymph node dissection and adjuvant management. Recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) were calculated. RESULTS: A total of 525 patients (88 younger patients and 437 older patients, matched 1:5) were included in this study. The two groups were well balanced except for less myometrial invasion in the younger patients. There were no significant differences between younger and older patients in regards to 5-year RFS (94% vs. 91%, p=0.6902). Similarly, there was no significant difference in regards to DSS (96% vs. 97%, p=0.9000). While 5-year OS was similar for both groups (89% vs. 89%, p=0.9942), 10-year OS was longer in the younger group (83% vs. 68% with p=0.13). On multivariate analysis for RFS, the presence of lymphovascular space invasion was the only predictor of shorter RFS (p=0.0007). Tumor grade (p=0.0002) and lower uterine segment involvement (p=0.0141) were independent predictors of shorter DSS. Older age (p<0.001) and stage II (p=0.01) were the only predictors of shorter OS. CONCLUSIONS: When matched based on tumor stage, grade and adjuvant management, our study suggests that there is no difference in survival endpoints between younger and older patients with early stage endometrial carcinoma.

Radiation Oncology

Karam I, Yao M, Heron DE, Poon I, Koyfman SA, Yom SS, **Siddiqui F**, Lartigau E, Cengiz M, Yamazaki H, Hara W, Phan J, Vargo JA, Lee V, Foote RL, Harter KW, Lee NY, Sahgal A, and Lo SS. Survey of current practices from the international stereotactic body radiotherapy consortium (isbrtc) for head and neck cancers *Future Oncol* 2016;PMID: 27842456. Article Request Form

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Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA.
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AIM: To provide a multi-institutional description of current practices of stereotactic body radiotherapy (SBRT) for head and neck cancer. MATERIALS & METHODS: 15 international institutions with significant experience in head and neck SBRT were asked to complete a questionnaire covering clinical and technical factors. RESULTS: SBRT is used 10-100% of the time for recurrent primary head and neck cancer, and 0-10% of the time in newly diagnosed disease. Five centers use a constraint for primary disease of 3-5 cm and 25-30 cc. Nine institutions apply a clinical target volume expansion of 1-10 mm and 14 use a planning target volume margin of 1-5 mm. Fractionation regimens vary between 15 and 22 Gy in 1 fraction to 30-50 Gy in 5 or 6 fractions. The risk of carotid blowout quoted in the re-irradiation setting ranges from 3 to 20%. CONCLUSION: There is considerable heterogeneity in patient selection and techniques in head and neck SBRT practice among experienced centers.

Radiation Oncology

Ross Green W, Hathout L, Khan AJ, **Elshaikh MA**, Beriwal S, Small W, Jr., and Mahmoud O. Revisiting Milan cervical cancer study: Do the original findings hold in the era of chemotherapy? *Gynecol Oncol* 2016;PMID: 27899201. Full Text

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BACKGROUND: The primary treatment of early stage cervical carcinoma (IB-IIA) is either surgery or radiation therapy based on the pivotal Milan randomized study published twenty years ago. In the presence of high-risk features, the gold standard treatment is concurrent chemotherapy and radiation therapy (CRT) whether it is the in the postoperative or the definitive setting. Using the National Cancer Data Base (NCDB), the goal of our study is to compare the outcomes of surgery and radiation therapy in the chemotherapy era. METHODS: Between 2004 and 2013, 5478 patients diagnosed with early stage cervical cancer were divided into 2 groups based on their primary treatment: non-surgical (n=1980) and surgical groups (n=3498). The distribution of patient/tumor characteristics and treatment variables with their relation to overall survival and proportional regression models were assessed to investigate the superiority of one approach over the other. Propensity score analysis adjusted for imbalance of covariates to create a well-matched-patient cohort. FINDINGS: At 46months median follow-up, the 5-year overall survival was similar between both groups (73.8% vs. 75.7%; p=0.619) after applying propensity score analysis. On multivariate analysis, high Charlson comorbidity score, stage IIA disease, larger tumor size, positive lymph nodes and high-grade disease were significant predictors of poor outcome while older age and treatment approach were not. INTERPRETATION: Our analysis suggests that surgery (followed by adjuvant RT or CRT) and definitive radiotherapy (with or without chemotherapy) result in equivalent survival. Prospective studies are warranted to establish this paradigm in the chemotherapy era.

Radiology

Siegal D, **Davis L**, **Scheer M**, and **Walker L**. Entrapment neuropathies of the upper extremity nerves *Current Radiology Reports* 2016; 4(12)PMID: Not assigned. Article Request Form

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Purpose of Review: This article reviews recent updates in the imaging for diagnosis and characterization of upper extremity nerve entrapments (UENE). We examine in detail the use of ultrasound and MRI, including state-of-the-art techniques such as dynamic nerve motion assessment, tissue elasticity measurement, and MR neurography. Recent Findings: Ultrasound and MRI are the two advanced modalities most frequently used to assess UENE. MRI remains technically challenging, though techniques of MR neurography have steadily improved. Ultrasound is operator-dependent, but has dynamic and realtime imaging capabilities and no contraindications. New comparative techniques of measurement and elasticity assessment show promise for improved diagnostic accuracy. Summary: Up-to-date imaging techniques for peripheral nerves in the upper extremity from the shoulder to the hand are discussed, with a focus on the most common UENE such as carpal tunnel syndrome and cubital tunnel syndromes. Technical challenges and limitations are reviewed, with a focus on the current and future state of imaging for UENE.

Radiology

Wang DD, **Eng M**, **Kupsky D**, **Myers E**, **Forbes M**, **Rahman M**, **Zaidan M**, **Parikh S**, **Wyman J**, **Pantelic M**, **Song T**, **Nadig J**, **Karabon P**, **Greenbaum A**, and **O'Neill W**. Application of 3-dimensional computed tomographic image guidance to WATCHMAN implantation and impact on early operator learning curve: Single-center experience *JACC Cardiovasc Interv* 2016; 9(22):2329-2340. PMID: 27884358. Full Text

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OBJECTIVES: The aim of this study was to examine the impact of 3-dimensional (3D) computed tomographic (CT) guided procedural planning for left atrial appendage (LAA) occlusion on the early operator WATCHMAN learning

curve. BACKGROUND: Traditional WATCHMAN implantation is dependent on 2-dimensional transesophageal echocardiographic (TEE) sizing and intraprocedural guidance. METHODS: LAA occlusion with the WATCHMAN device was performed in 53 patients. Pre-procedural case plans were generated from CT studies with recommended device size, catheter selection, and C-arm angle for deployment. RESULTS: All 53 patients underwent successful LAA occlusion with the WATCHMAN. Three-dimensional CT LAA maximal-width sizing was 2.7 +/- 2.2 mm and 2.3 +/- 3.0 mm larger than 2-dimensional and 3D TEE measurements, respectively (p </= 0.0001). By CT imaging, device selection was 100% accurate. There were 4 peri-WATCHMAN leaks (<4.5 mm) secondary to accessory LAA pedunculations. By 2-dimensional TEE maximal-width measurements alone, 62.3% (33 of 53) would have required larger devices. Using 3D TEE maximal-width measurements, 52.8% of cases (28 of 53) would have required larger devices. Three-dimensional TEE length would have inappropriately excluded 10 patients from WATCHMAN implantation. Compared with the average of 1.8 devices used per implantation attempt in PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) (82% success rate), the present site averaged 1.245 devices per implantation attempt (100% success rate). There were no intraprocedural screen failures and no major adverse cardiac events. CONCLUSIONS: Three-dimensional CT image case planning provides a comprehensive and customized patient-specific LAA assessment that appears to be accurate and may possibly facilitate reducing the early WATCHMAN implantation learning curve.

Research
MaBouDi H, Shimazaki H, Amari S, and **Soltanian-Zadeh H**. Representation of higher-order statistical structures in natural scenes via spatial phase distributions *Vision Res* 2016; 120:61-73. PMID: 26278166. Article Request Form

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Natural scenes contain richer perceptual information in their spatial phase structure than their amplitudes. Modeling phase structure of natural scenes may explain higher-order structure inherent to the natural scenes, which is neglected in most classical models of redundancy reduction. Only recently, a few models have represented images using a complex form of receptive fields (RFs) and analyze their complex responses in terms of amplitude and phase. However, these complex representation models often tacitly assume a uniform phase distribution without empirical support. The structure of spatial phase distributions of natural scenes in the form of relative contributions of paired responses of RFs in quadrature has not been explored statistically until now. Here, we investigate the spatial phase structure of natural scenes using complex forms of various Gabor-like RFs. To analyze distributions of the spatial phase responses, we constructed a mixture model that accounts for multi-modal circular distributions, and the EM algorithm for estimation of the model parameters. Based on the likelihood, we report presence of both uniform and structured bimodal phase distributions in natural scenes. The latter bimodal distributions were symmetric with two peaks separated by about 180 degrees . Thus, the redundancy in the natural scenes can be further removed by using the bimodal phase distributions obtained from these RFs in the complex representation models. These results predict that both phase invariant and phase sensitive complex cells are required to represent the regularities of natural scenes in visual systems.

Research
Maleki-Balajoo S, Hossein-Zadeh GA, **Soltanian-Zadeh H**, and Ekhtiari H. Locally estimated hemodynamic response function and activation detection sensitivity in heroin-cue reactivity study *Basic Clin Neurosci* 2016; 7(4):299-314. PMID: 27872691. Full Text

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INTRODUCTION: A fixed hemodynamic response function (HRF) is commonly used for functional magnetic resonance imaging (fMRI) analysis. However, HRF may vary from region to region and subject to subject. We

investigated the effect of locally estimated HRF (in functionally homogenous parcels) on activation detection sensitivity in a heroin cue reactivity study. METHODS: We proposed a novel exploratory method for brain parcellation based on a probabilistic model to segregate the brain into spatially connected and functionally homogeneous components. Then, we estimated HRF and detected activated regions in response to an experimental task in each parcel using a joint detection estimation (JDE) method. We compared the proposed JDE method with the general linear model (GLM) that uses a fixed HRF and is implemented in FEAT (as a part of FMRIB Software Library, version 4.1). RESULTS: 1) Regions detected by JDE are larger than those detected by fixed HRF, 2) In group analysis, JDE found areas of activation not detected by fixed HRF. It detected drug craving a priori "regions-of-interest" in the limbic lobe (anterior cingulate cortex [ACC], posterior cingulate cortex [PCC] and cingulate gyrus), basal ganglia, especially striatum (putamen and head of caudate), and cerebellum in addition to the areas detected by the fixed HRF method, 3) JDE obtained higher Z-values of local maxima compared to those obtained by fixed HRF. CONCLUSION: In our study of heroin cue reactivity, our proposed method (that estimates HRF locally) outperformed the conventional GLM that uses a fixed HRF.

Sleep Medicine
Palagini L, Mauri M, Dell'Osso L, Riemann D, and **Drake CL**. Trait- and pre-sleep-state-dependent arousal in insomnia disorders: what role may sleep reactivity and sleep-related metacognitions play? A pilot study *Sleep Med* 2016; 25:42-48. PMID: 27823715. Full Text

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OBJECTIVE: Research into the cause of chronic insomnia has identified hyperarousal as a key factor, which is likely to have both trait and state components. Sleep-related cognition, metacognition, and sleep reactivity also play an important role in insomnia. Our aim was to investigate how these insomnia-related constructs are associated with trait predisposition and pre-sleep arousal in subjects with an insomnia disorder. METHODS: Fifty-three individuals with insomnia disorder (according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (F = 33; 52 + 10)) and 30 healthy controls (F = 18; 51.8 + 12 years) were evaluated with a set of questionnaires, including the Ford Insomnia Response to Stress Test (FIRST), Metacognition Questionnaire - Insomnia (MCQI), Arousal Predisposition Scale (APS), and Pre-sleep Arousal Scale (PSAS). Statistical analyses included multiple regression to elucidate the independent determinants of APS and PSAS. RESULTS: Participants with insomnia presented higher FIRST, MCQI, APS, PSAS scores (p-values <0.001) than healthy controls. In insomnia, APS and cognitive PSAS were best determined by MCQI (respectively, B = 0.09, p = 0.001, B = 0.08, p = 0.02), somatic PSAS by cognitive arousal (PSAS B = 0.35, p = 0.004) CONCLUSIONS: This study suggests that in insomnia disorders, trait predisposition toward hyperarousal and pre-sleep-cognitive-state-dependent arousal may be closely related to sleep-related metacognitive processes. Sleep-related metacognitive processes may be associated with trait hyperarousal within the framework of a mutual relationship, and could, in turn, modulate cognitive pre-sleep-state arousal. A broad range of cognitive and metacognitive processes should be considered when dealing with subjects with insomnia.

Sleep Medicine
Roth T, Dauvilliers Y, Guinta D, Alvarez-Horine S, Dynin E, and Black J. Effect of sodium oxybate on disrupted nighttime sleep in patients with narcolepsy *J Sleep Res* 2016;PMID: 27807903. Full Text

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This post hoc analysis evaluated the dose-related effects of sodium oxybate on sleep continuity and nocturnal sleep quality in patients with narcolepsy-cataplexy. Polysomnography data, including shifts to Stage N1/Wake, were from a randomized, placebo-controlled trial of sodium oxybate. Patients were >/=16 years old with a diagnosis of narcolepsy including symptoms of cataplexy and excessive daytime sleepiness. Treatment was for 8 weeks with placebo or sodium oxybate 4.5, 6 or 9 g administered as two equally divided nightly doses. Relative to baseline, significant dose-dependent reductions in the number of shifts per hour from Stages N2/3/rapid eye movement and Stages N2/3 to Stage N1/Wake were observed at week 8 with sodium oxybate (P < 0.05); sodium oxybate 6- and 9-g doses also

resulted in similar reductions in shifts per hour of rapid eye movement to Stage N1/Wake (both P < 0.05). Across all shift categories, the shift reductions with sodium oxybate 9 g were significantly greater than those observed with placebo (P < 0.05). Improvements from baseline in reported sleep quality were significantly greater with sodium oxybate 4.5 and 9 g at week 8 (P < 0.05). Correlations between change from baseline in number of shifts per hour to Stage N1/Wake and cataplexy frequency, patient-reported nocturnal sleep quality, and excessive daytime sleepiness assessed using the Epworth Sleepiness Scale were numerically highest for the sodium oxybate 9-g dose across all sleep stage shift categories. In these patients with narcolepsy, sodium oxybate showed improvements in the sleep continuity and nocturnal sleep quality that are characteristic of disrupted nighttime sleep (ClinicalTrials.gov identifier NCT00049803).

Surgery

D'Agostino RS, Jacobs JP, Badhwar V, **Paone G**, Rankin JS, Han JM, McDonald D, Edwards FH, and Shahian DM. The society of thoracic surgeons adult cardiac surgery database: 2017 update on outcomes and quality *Ann Thorac Surg* 2016;PMID: 27884412. Full Text

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Established in 1989, The Society of Thoracic Surgeons Adult Cardiac Surgery Database is one of the most comprehensive clinical data registries in health care. It is widely regarded as the gold standard for benchmarking risk-adjusted outcomes in cardiac surgery and is the foundation for all quality measurement and improvement activities of The Society of Thoracic Surgeons. This is the second in a series of annual reports that summarizes current aggregate national outcomes in cardiac surgery and reviews database-related activities in the areas of quality measurement and performance improvement during the past year.

Surgery

Henke PK, Park YJ, **Hans S**, Bove P, Cuff R, Kazmers A, Schreiber T, Gurm HS, and Grossman PM. The association of peri-procedural blood transfusion with morbidity and mortality in patients undergoing percutaneous lower extremity vascular interventions: Insights from BMC2 VIC *PLoS One* 2016; 11(11):e0165796. PMID: 27835656. Full Text

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OBJECTIVE: To determine the predictors of periprocedural blood transfusion and the association of transfusion on outcomes in high risk patients undergoing endoluminal percutaneous vascular interventions (PVI) for peripheral arterial disease. METHODS/RESULTS: Between 2010-2014 at 47 hospitals participating in a statewide quality registry, 4.2% (n = 985) of 23,273 patients received a periprocedural blood transfusion. Transfusion rates varied from 0 to 15% amongst the hospitals in the registry. Using multiple logistic regression, factors associated with increased transfusion included female gender (OR = 1.9; 95% CI: 1.6-2.1), low creatinine clearance (1.3; 1.1-1.6), pre-procedural anemia (4.7; 3.9-5.7), family history of CAD (1.2; 1.1-1.5), CHF (1.4; 1.2-1.6), COPD (1.2; 1.1-1.4), CVD or TIA (1.2; 1.1-1.4), renal failure CRD (1.5; 1.2-1.9), pre-procedural heparin use (1.8; 1.4-2.3), warfarin use (1.2; 1.0-1.5), critical limb ischemia (1.7; 1.5-2.1), aorta-iliac procedure (1.9; 1.5-2.5), below knee procedure (1.3; 1.1-1.5), urgent procedure (1.7; 1.3-2.2), and emergent procedure (8.3; 5.6-12.4). Using inverse weighted propensity matching to adjust for confounders, transfusion was a significant risk factor for death (15.4; 7.5-31), MI (67; 29-150), TIA/stroke (24; 8-73) and ARF (19; 6.2-57). A focused QI program was associated with a 28% decrease in administration of

blood transfusion (p = 0.001) over 4 years. CONCLUSION: In a large statewide PVI registry, post procedure transfusion was highly correlated with a specific set of clinical risk factors, and with in-hospital major morbidity and mortality. However, using a focused QI program, a significant reduction in transfusion is possible.

Surgery
Jacobs JP, Shahian DM, Prager RL, Edwards FH, McDonald D, Han JM, D'Agostino RS, Jacobs ML, Kozower BD, Badhwar V, Thourani VH, Gaissert HA, Fernandez FG, Wright CD, **Paone G**, Cleveland JC, Jr., Brennan JM, Dokholyan RS, Brothers L, Vemulapalli S, Habib RH, O'Brien SM, Peterson ED, Grover FL, Patterson GA, and Bavaria JE. The society of thoracic surgeons national database 2016 annual report *Ann Thorac Surg* 2016; 102(6):1790-1797. PMID: 27847042. Full Text

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The art and science of outcomes analysis, quality improvement, and patient safety continue to evolve, and cardiothoracic surgery leads many of these advances. The Society of Thoracic Surgeons (STS) National Database is one of the principal reasons for this leadership role, as it provides a platform for the generation of knowledge in all of these domains. Understanding these topics is a professional responsibility of all cardiothoracic surgeons. Therefore, beginning in January 2016, The Annals of Thoracic Surgery began publishing a monthly series of scholarly articles on outcomes analysis, quality improvement, and patient safety. This article provides a summary of the status of the STS National Database as of October 2016 and summarizes the articles about the STS National Database that appeared in The Annals of Thoracic Surgery 2016 series, "Outcomes Analysis, Quality Improvement, and Patient Safety."

Surgery
Karamanos E, **Kandagatla P**, **Watson J**, **Schmoekel N**, and **Siddiqui A**. Development and validation of a scoring system to predict surgical site infection after ventral hernia repair: A michigan surgical quality collaborative study *World J Surg* 2016;PMID: 27872976. Full Text

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INTRODUCTION: Surgical site infections (SSIs) are a rare but significant complication following an elective ventral hernia repair. This study aims to develop a risk assessment tool in order to predict the risk of developing SSIs postoperatively. METHODS: All patients undergoing an elective ventral hernia repair were identified using the Michigan Surgical Quality Collaborative (MSQC) database. Patients' demographics, comorbidities and technical aspects of the operations were extracted. Logistic regressions were used to create a predictive scoring system for SSIs. RESULTS: A total of 4983 were included. SSIs occurred in 3.4% of the patient population. A stepwise forward logistic regression identified the need to use drains, BMI, wound classification at the end of the surgery, presence of severe adhesions, a history of CAD, the need for intensive care after surgery, the use of pressors, EtOH abuse and

history of PVD as being independently associated with the development of postoperative surgical site infections. CONCLUSION: In patients undergoing an elective hernia repair, the incidence of SSI is low. Several preoperative and perioperative factors can contribute to the development of SSIs.

Surgery
Liu Y, **Gao X**, **Deeb D**, **Zhang Y**, **Shaw J**, **Valeriote FA**, and **Gautam SC**. Mycotoxin verrucarin A inhibits proliferation and induces apoptosis in prostate cancer cells by inhibiting prosurvival Akt/NF-kB/mTOR signaling *J Exp Ther Oncol* 2016; 11(4):251-260. PMID: 27849335. Article Request Form

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Trichothecenes are powerful mycotoxins that inhibit protein synthesis and induce ribotoxic stress response in mammalian cells. Verrucarin A (VC-A) is a Type D macrocyclic mycotoxin which inhibits cell proliferation and induces apoptosis in cancer cells. However, the antitumor activity of VC-A for prostate cancer cells has not been investigated. The objective of the present study was to determine the anticancer activity and its mechanism of action in hormone-responsive (LNCaP) and hormone-refractory (PC-3) carcinoma of the prostate (CaP) cell lines. VC-A strongly inhibited the proliferation and induced cell cycle arrest in G2/M phase associated with the inhibition of cell cycle regulatory proteins cyclin D, cyclin E, cyclin-dependent kinases (cdks) cdk2, cdk4, cdk6 and cdk inhibitors WAF1/21 and KIP1/27. VC-A also induced apoptosis in CaP cells as characterized by the cleavage of poly (ADP-ribose) polymerase (PARP-1), procaspases-3, -8 and -9 and the inhibition of Bcl-2 family proteins that regulate apoptosis (Bcl-2, Bcl-xL, Bax, Bak and Bad). In addition, VC-A also down-regulated the expression of prosurvival phospho-AKT (p-AKT), nuclear factor kappa B (NF-kB) (p65) and phospho-mammalian target of rapamycin (p-mTOR) signaling proteins. Taken together, these results demonstrated strong antiproliferative and apoptosis-inducing activity of verrucarin A against CaP cells through cell cycle arrest and inhibition of the prosurvival (antiapoptotic) AKT/NF-kB/mTOR signaling pathway.

Surgery
Macedo M, **Kim B**, **Khoury R**, and **Narkiewicz L**. A rare case of right lower quadrant abdominal pain *Am J Emerg Med* 2016;PMID: 27842925. Full Text

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Isolated fallopian tube torsion without involvement of the ovary is a rare condition most frequently presenting during reproductive years. Imaging, vitals, physical exam, and laboratory findings all fail to help establish a definitive diagnosis. The majority of the diagnoses are made on the operating table. Physical exam most often reveals unilateral and localized abdominal pain, often with nausea and vomiting, but few other reliably common findings. Diagnosis becomes even more challenging due to the fact that isolated tubal torsion occurs often in pregnancy and preferentially on the right, further complicating the clinical picture. We describe a case of isolated tubal torsion, unique in that localized necrosis and inflammation from the torsion triggered a secondary appendicitis. The patient required surgical intervention, and an appendectomy and salpingectomy emergently. Given its elusive and rare nature, awareness and early intervention is required by the emergency physician to recognize tubal torsion, as operative intervention is crucial, and can lead to preservation of fertility and improved fetal survival.

Surgery
Moonka D, **Nagai S**, **Divine G**, and **Salgia R**. Influence of donor age and cold ischemia on recurrence of hepatocellular carcinoma after liver transplantation *Transplantation* 2016; 100(7):S427. PMID: Not assigned. Abstract

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Introduction: The role of donor age on recurrence of hepatocellular carcinoma (HCC) after liver transplant (LT) is not clear. In the current analysis, we evaluate the impact of donor age and cold ischemia time on HCC recurrence after LT. Methods: We evaluated 303 consecutive LT patients at our institution with HCC. Nine were excluded because of

findings of cholangiocarcinoma, 11 were excluded because of death within three months and one because of positive HCC margins at LT leaving 282 patients. . Patients were evaluated for a variety of factors for association with time to HCC recurrence using Kaplan-Meier estimates and logrank tests. Multivariate modeling was done using Cox regression analysis. Results and Discussion: In the 282 patients, there were 41 HCC recurrences (14.5%) occurring at a median of 17 months and a mean of 22.2 months and a range of 22 to 98 months. On univariate analysis, factors associated with HCC recurrence were cold ischemia (P < 0.001), donor age (P=0.025), tumor burden within Milan criteria on explant (P < 0.001), maximum alpha-fetoprotein (AFP) (P=0.005) and AFP at time of LT (P < 0.001), poorly differentiated histology (P < 0.001), vascular invasion (P < 0.001) and percent necrosis (P=0.017) in those undergoing pre-LT treatment. Patients with HCC recurrence had a donor age of 47.0 ± 16.7 and those without had a donor age of 41.2 ± 16.2 (P=0.038). Patients with recurrence had a cold ischemia time in hours of 6.8 ± 2.1 vs 5.6 ± 1.7 in those without (P=0.001). For both donor age and cold ischemia, the Youden's J statistic was used to determine an optimal cutoff to discriminate between patients with and without recurrence. The 209 patients with donors less than 55 years old had 1, 3 and 5 year tumor free survival of 93.7%, 90.2% and 87.3% vs 91.5%, 78.4% and 70.3% in the 73 patients with donors over 55 (P=0.009). The 119 patients with cold ischemia less than 5.5 hours had 1, 3 and 5 year tumor free survival of 95.8%, 92.6% and 91.0% vs 91.2%, 82.7% and 76.6% in the 150 patients over 5.5 hours (P=0.006). The 37 patients with donors over 55 and cold ischemia over 5.5 hours had 1, 3 and 5 year tumor free survival of 88.7%, 67.0% and 57.4% vs 95.4%, 92.5%, and 92.5% for the 88 patients with both lower donor age and shorter cold ischemia. In a multivariate analysis controlling for tumor burden, histology and vascular invasion: donor age (P=0.007), cold ischemia (P=0.005), Milan criteria on explant (P=0.002), maximum AFP (P=0.016), AFP at OLT (P=0.004), poorly differentiated histology (P < 0.001) and vascular invasion (P=0.002) were associated with time to tumor recurrence Conclusions: Both lower donor age and shorter cold ischemia time were independently associated with improved tumor free survival after liver transplant. If confirmed in larger cohorts, these represent potentially modifiable factors in liver transplant patients with liver cancer.

Surgery

Moonka D, **Nagai S**, **Gadde R**, **Datta L**, **Divine G**, **Abouljoud MS**, and **Salgia R**. Effect of tumor necrosis from loco-regional therapy prior to liver transplantation on hepatocellular carcinoma recurrence after transplant *Hepatology* 2016; 63(1):640A-641A. PMID: Not assigned. Abstract

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Few studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on recurrence of hepatocellular carcinoma (HCC) after LT. We describe results in 181 LT patients. Methods: We evaluated 260 consecutive LT patients with presumed HCC. Patients were excluded for cholangiocarcinoma (9), death within 3 months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients. Patients were evaluated for factors associated with time to HCC recurrence using Kaplan-Meier estimates with log-rank test. Multivariate modeling used Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had 1 treatment, 25 had 2 and 4 had 3 treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium-90 embo-lization. 30 patients had HCC recurrence at a mean of 24.0 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without (P=0.023). A cutoff of 85% necrosis gave a maximal Youden's J statistic for discriminating groups less likely to recur from those more likely. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For 114 patients with < 85% necrosis, 1, 3 and 5 year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant in part because all patients with > 85% necrosis were within Milan. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Surgery

Moonka D, **Shah V**, **Datta L**, **Gadde R**, **Divine G**, **Yoshida A**, **Jafri SM**, and **Salgia R**. Degree of tumor necrosis from pre-transplant loco-regional therapy is associated with tumor free survival after liver transplantation *Transplantation* 2016; 100(7):S429. PMID: Not assigned. Abstract

D. Moonka, Gastroenterology and Hepatology, Henry Ford Health System, Detroit, United States

Introduction: Previous studies have looked at the impact of tumor necrosis from loco-regional therapy (LRT) prior to liver transplant (LT) on the rate of recurrence of hepatocellular carcinoma (HCC) after transplant. These studies have shown mixed results. We describe our results in 181 LT patients with HCC at our center. Methods: We evaluated 260 consecutive LT patients at our institution with known HCC. Patients were excluded for cholangiocarcinoma (9), death within three months (11), residual cancer after LT (1), no LRT (47) or unavailable necrosis data (11). This left 181 patients of whom 30 had HCC recurrence. Patients were evaluated for a variety of factors for association with time to HCC recurrence using Kaplan-Meier estimates and log-rank tests. Multivariate modeling was done using Cox regression analysis. Results and Discussion: Of 181 LT patients, 152 patients had one treatment, 25 had two and four patients had three treatments. There were 70 ablations, 80 chemoembolization, 47 bland embolization and 10 yttrium (Y-90) embolization. Thirty patients had HCC recurrence at a mean of 24.0 months with a range of 3.4 to 97.6 months. On univariate analysis, factors associated with time to HCC recurrence were percent necrosis (P=0.016), longer cold ischemia time (P=0.008), older donor age (P=0.050), tumor exceeding Milan criteria on explant (P<0.001), maximum AFP (P=0.015), poorly differentiated histology (P=0.027) and vascular invasion (P=0.007). The type of LRT was not associated with time to recurrence. Patients with HCC recurrence had a mean percent necrosis of 52.7 ± 32.7% compared to 67.7 ± 33.5% for patients without recurrence (P=0.023). A cutoff of 85% tumor necrosis gave the maximal Youden's J statistic for discriminating groups most likely to recur from those less likely to do so. 77 patients had > 85% necrosis and their 1, 3 and 5 year tumor free survival was 94.7%, 94.7% and 92.9%. For the 114 patients with < 85% necrosis, 1, 3 and 5 year tumor free survival was 91.3%, 80.1% and 71.6%. The difference between the two curves is significant at P=0.002. On multivariate analysis, percent tumor necrosis was no longer a significant predictor of time to recurrence (P=0.117) when controlling for whether tumor burden met Milan criteria on explant. Of note, all patients with > 85% necrosis were within Milan criteria on explant. However, percent necrosis remained significant when controlling for pre-transplant variables of tumor within Milan criteria on pre-LT imaging and maximum AFP prior to LT (P=0.012). Cold ischemia time, maximum AFP, poorly differentiated histology, Milan criteria and vascular invasion remained significant in multivariate models. Conclusions: In patients undergoing LRT, the percent necrosis is associated with tumor free recurrence with near complete necrosis of over 85% demonstrating the best efficacy. These results highlight the importance of effective LRT prior to transplant in patients with liver cancer.

Surgery

O'Connell PJ, Busque S, Vincenti F, Tedesco Silva H, **Yoshida A**, Friedewald JJ, Steinberg SJ, Budde K, Broeders EN, Kim YS, Hahn C, Li H, and Chan G. Tofacitinib in renal allograft recipients: Long-term efficacy and safety in an active-comparator-controlled extension trial *Transplantation* 2016; 100(7):S84-S85. PMID: Not assigned. Abstract

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Introduction: Tofacitinib is an oral Janus kinase inhibitor. In a Phase 2b study, tofacitinib was effective in preventing acute renal allograft rejection in the first 12 months (mos) post-transplant but with an increased risk of serious infection events (SIEs) and three cases of post transplant lymphoproliferative disease (PTLD)[1]. Here we evaluate the long-term efficacy and safety of tofacitinib in renal allograft patients (pts) over the next 60 mos. Materials and Methods: Kidney transplant pts who completed 12 mos of randomised treatment with cyclosporine (CsA) or a Less Intensive (LI) or More Intensive (MI) tofacitinib regimen were enrolled in a Phase 2b, open-label extension study (NCT00658359). Pts continued their previous treatment of CsA or tofacitinib with mycophenolic acid products for 5 years, through Mo 72 post-transplant. Pts receiving tofacitinib MI/LI continued 10 mg twice daily (BID), decreasing to 5 mg BID by Mo 18. Primary outcomes were the incidence of first biopsy-proven acute rejection (BPAR), treated clinical acute rejection and adverse events (AEs). Secondary outcomes included glomerular filtration rate (GFR), chronic allograft nephropathy (CAN) and pt and allograft survival. Results: 178 pts were enrolled (CsA: n=64; tofacitinib LI: n=60; tofacitinib MI: n=54). Pt demographics were similar in all groups. Clinical outcomes are presented in Table 1. All groups had a similar BPAR rate but the treated clinical acute rejection rate was higher for CsA vs tofacitinib (CsA 29.7%, LI 11.7%, MI 11.1%). Estimated GFR was higher in tofacitinib pts than CsA pts by 10-15 mL/min/1.73m2 but the rate of CAN was ≥60% in all groups. Pt and allograft survival rates, and AE and serious AE frequencies were comparable among groups. The SIE rates were: CsA 28.1%, LI 35.0% and MI 25.9%. The rates of malignancies were: CsA 9.4%, LI 10.0% and MI 14.8%. Two new cases of PTLD occurred in the tofacitinib MI group after Mo 12 posttransplant. A protocol amendment was implemented to discontinue 43 pts who had above-median tofacitinib exposure in the first 12 mos posttransplant, since all 5 cases of PTLD occurred in above-median exposure pts. No PTLD cases occurred in pts who continued after the protocol amendment. Conclusion: Long-term tofacitinib treatment was effective in preventing acute allograft rejection. At Mo 72, tofacitinib pts had better renal function but similar cumulative CAN rates vs CsA. Long-term SIE risk remained but the magnitude of risk relative to CsA was reduced vs the first 12 mos post-transplant. Above-median tofacitinib exposure appears to be associated with increased PTLD risk. No new safety signals were reported. (Table Presented).

Surgery

Pahari H, Chaudhary RJ, Thiagarajan S, Raut V, Babu R, Bhangui P, Goja S, Rastogi A, Vohra V, and Soin AS. Hepatic venous and inferior vena cava morphology no longer a barrier to living donor liver transplantation for budd-chiari syndrome: Surgical techniques and outcomes *Transplant Proc* 2016; 48(8):2732-2737. PMID: 27788809. Full Text

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BACKGROUND: Living donor liver transplantation (LDLT) for Budd-Chiari syndrome (BCS) has been reported with <10 inferior vena cava (IVC) replacements with vascular/synthetic graft. The goal of this study was to review outcomes of LDLT for BCS at our center, with an emphasis on surgical techniques and postoperative anticoagulation therapy. METHODS: Between October 2011 and December 2015, a total of 1027 LDLTs were performed. Nine of these patients had BCS. We analyzed their etiologies, operative details, postoperative complications, and outcomes. RESULTS: The indication was chronic liver disease for all patients. Two patients required retrohepatic IVC replacement with a polytetrafluoroethylene graft due to severe adhesions and thrombosis, respectively. One patient required V-Y plasty for suprahepatic IVC narrowing. Five patients had portal venous thrombosis, 3 treated by thrombectomy, and 1 by renoportal anastomosis. The mean follow-up time was 18 +/- 16 months. Only 1 early death occurred due to sepsis. The anticoagulation therapy involved heparin infusion from postoperative day 1, conversion to low-molecular-weight-heparin on postoperative days 3 to 6, followed by warfarin (postoperative days 9-16 to maintain an international normalized ratio of 2-3 long term), along with low-dose aspirin for 6 months. There was no recurrence of thrombosis. CONCLUSIONS: LDLT for BCS is well documented in literature. Prevention of recurrent thrombosis depends on meticulous surgical technique, perfect and wide outflow anastomoses, and a strict anticoagulation protocol. A synthetic (polytetrafluoroethylene) graft for IVC interposition is a safe and feasible option for reconstruction with good results. Low-dose aspirin with low-molecular-weight-heparin later converted to warfarin provides excellent results and prevents recurrence of thrombosis.

Surgery

Wang DD, **Eng M**, **Kupsky D**, **Myers E**, **Forbes M**, **Rahman M**, **Zaidan M**, **Parikh S**, **Wyman J**, **Pantelic M**, **Song T**, **Nadig J**, **Karabon P**, **Greenbaum A**, and **O'Neill W**. Application of 3-dimensional computed tomographic image guidance to WATCHMAN implantation and impact on early operator learning curve: Single-center experience *JACC Cardiovasc Interv* 2016; 9(22):2329-2340. PMID: 27884358. Full Text

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OBJECTIVES: The aim of this study was to examine the impact of 3-dimensional (3D) computed tomographic (CT) guided procedural planning for left atrial appendage (LAA) occlusion on the early operator WATCHMAN learning curve. BACKGROUND: Traditional WATCHMAN implantation is dependent on 2-dimensional transesophageal echocardiographic (TEE) sizing and intraprocedural guidance. METHODS: LAA occlusion with the WATCHMAN device was performed in 53 patients. Pre-procedural case plans were generated from CT studies with recommended device size, catheter selection, and C-arm angle for deployment. RESULTS: All 53 patients underwent successful LAA occlusion with the WATCHMAN. Three-dimensional CT LAA maximal-width sizing was 2.7 +/- 2.2 mm and 2.3 +/- 3.0 mm larger than 2-dimensional and 3D TEE measurements, respectively (p </= 0.0001). By CT imaging, device selection was 100% accurate. There were 4 peri-WATCHMAN leaks (<4.5 mm) secondary to accessory LAA pedunculations. By 2-dimensional TEE maximal-width measurements alone, 62.3% (33 of 53) would have required larger devices. Using 3D TEE maximal-width measurements, 52.8% of cases (28 of 53) would have required larger devices. Three-dimensional TEE length would have inappropriately excluded 10 patients from WATCHMAN implantation. Compared with the average of 1.8 devices used per implantation attempt in PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) (82% success rate), the present site averaged 1.245 devices per implantation attempt (100% success rate). There were no intraprocedural screen failures and no major adverse cardiac events. CONCLUSIONS: Three-dimensional CT image case planning provides a comprehensive and customized patient-specific LAA assessment that appears to be accurate and may possibly facilitate reducing the early WATCHMAN implantation learning curve.

Urology
Dalela D, **Karabon P**, and **Abdollah F**. Androgen deprivation therapy and dose-escalated radiotherapy for intermediate- and high-risk prostate cancer: Sign of changing times? *JAMA Oncol* 2016;PMID: 27893042. Full Text

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Urology
Hussein AA, Ghani KR, **Peabody J**, Sarle R, Abaza R, Eun D, Hu J, **Fumo M**, Lane B, Montgomery J, Hinata N, Rooney D, Comstock B, Chan HK, Mane SS, Mohler JL, Wilding G, Miller D, and Guru KA. Development and validation of an objective scoring tool for robot-assisted radical prostatectomy: Prostatectomy assessment and competency evaluation (pace) *J Urol* 2016;PMID: 27913152. Full Text

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INTRODUCTION: and Background: Comprehensive training and skill acquisition by urologic surgeons are vital to optimize surgical outcomes and patient safety. We sought to develop and validate an objective and procedure specific tool to assess the quality of robot-assisted radical prostatectomy (RARP)-Prostatectomy Assessment and Competence Evaluation (PACE) METHODS: Development and content validation of PACE was performed by deconstruction of RARP into seven key domains utilizing the Delphi methodology. The reliability and construct validation were then assessed utilizing de-identified videos performed by practicing surgeons and fellows. Consensus for each domain was defined as achieving a content validity index (CVI) >/=0.75. Reliability was assessed using intra-class correlation (ICC) and construct validation using a mixed linear model accounting for multiple ratings on the same video. Consensus was reached after 3 rounds on wording, relevance of skills assessed, and concordance between the score assigned and the skill assessed. ICC >/= 0.4 was achieved for all domains. The expert group outperformed trainees in all domains but reached statistical significance in bladder drop (4.5 versus 3.4, p=0.002), preparation of the prostate (4.4 versus 3.2, p<0.0001), seminal vesicles and posterior plane dissection (8.3 versus 6.8, p=0.03) and neurovascular bundle preservation (4.1 versus 2.4, p<0.0001). Limitations include the lack of assessment of other key skills as communication and decision making. CONCLUSIONS: PACE is a structured, procedure-specific and reliable tool that objectively measures surgical performance during RARP. It can differentiate different levels of expertise, and provide structured feedback to customize training and surgical quality improvement.

Urology
Lovegrove C, Novara G, Mottrie A, Guru KA, Brown M, Challacombe B, Popert R, Raza J, Van der Poel H, **Peabody J**, Dasgupta P, and Ahmed K. Structured and modular training pathway for robot-assisted radical prostatectomy (rarp): Validation of the rarp assessment score and learning curve assessment *Eur Urol* 2016; 69(3):526-535. PMID: 26585582. Full Text

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BACKGROUND: Use of robot-assisted radical prostatectomy (RARP) for prostate cancer is increasing. Structured surgical training and objective assessment are critical for outcomes. OBJECTIVE: To develop and validate a modular training and assessment pathway via Healthcare Failure Mode and Effect Analysis (HFMEA) for trainees undertaking RARP and evaluate learning curves (LCs) for procedural steps. DESIGN, SETTING, AND PARTICIPANTS: This multi-institutional (Europe, Australia, and United States) observational prospective study used HFMEA to identify the high-risk steps of RARP. A specialist focus group enabled validation. Fifteen trainees who underwent European Association of Urology robotic surgery curriculum training performed RARP and were assessed by mentors using the tool developed. Results produced LCs for each step. A plateau above score 4 indicated competence. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We used a modular training and assessment tool (RARP Assessment Score) to evaluate technical skills. LCs were constructed. Multivariable Kruskal-Wallis, Mann-Whitney U, and kappa coefficient analyses were used. RESULTS AND LIMITATIONS: Five surgeons were observed for 42 console hours to map steps of RARP. HFMEA identified 84 failure modes and 46 potential causes with a hazard score >/=8. Content validation created the RARP Assessment Score: 17 stages and 41 steps. The RARP Assessment Score was acceptable (56.67%), feasible (96.67%), and had educational impact (100%). Fifteen robotic surgery trainees were assessed for 8 mo. In 426 RARP cases (range: 4-79), all procedural steps were attempted by trainees. Trainees were assessed with the RARP Assessment Score by their expert mentors, and LCs for individual steps were plotted. LCs demonstrated plateaus for anterior bladder neck transection (16 cases), posterior bladder neck transection (18 cases), posterior dissection (9 cases), dissection of prostatic pedicle and seminal vesicles (15 cases), and anastomosis (17 cases). Other steps did not plateau during data collection. CONCLUSIONS: The RARP Assessment Score based on HFMEA methodology identified critical steps for focused RARP training and assessed surgeons. LCs demonstrate the experience necessary to reach a level of competence in technical skills to protect patients. PATIENT SUMMARY: We developed a safety and assessment tool to gauge the technical skills of surgeons performing robot-assisted radical prostatectomy. Improvement was monitored, and measures of progress can be used in future to guide mentors when training surgeons to operate safely.

Urology

Macki M, and **Dabaja AA**. Literature review of vaccine-related adverse events reported from HPV vaccination in randomized controlled trials *Basic Clin Androl* 2016; 26:16. PMID: 27895921. Full Text

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BACKGROUND: The human papilloma virus (HPV) infections were addressed with two FDA-approved HPV vaccines: quadrivalent and bivalent vaccine. The objective of this manuscript is to determine the safety of the HPV vaccine. RESULTS: A search of PubMed articles for "human papillomavirus vaccine" was used to identify all-type HPV clinical studies prior to October 2014. A refined search of clinical trials, multicenter studies, and randomized studies were screened for only randomized controlled trials comparing HPV vaccine to controls (saline placebo or aluminum derivatives). Studies were limited to the two FDA-approved vaccines. Following PRISMA guidelines, the literature review rendered 13 publications that met inclusion/ exclusion criteria. Gender was limited to females in 10 studies and males in 1 study. Two studies included both males and females. Of the 11,189 individuals in 7 publications reporting cumulative, all-type adverse events (AE), the AE incidence of 76.52 % (n = 4544) in the vaccinated group was statistically significantly higher than 67.57 % (n = 3548) in the control group ($p < 0.001$). The most common AE were injection-site reactions. On the other hand, systemic symptoms did not statistically significantly differ between the vaccination cohort (35.28 %, n = 3351) and the control cohort (36.14 %, n = 3198) ($p = 0.223$). The pregnancy/ perinatal outcomes rendered no statistically significant difference between the vaccine group and control group. CONCLUSION: Because the statistically significantly higher incidence of AE in the HPV vaccine group was primarily limited to injection-site reactions, the vaccinations are safe preventative measures in both males and females.

Urology

Sarveswaran S, **Ghosh R**, **Parikh R**, and **Ghosh J**. Wedelolactone, an anti-inflammatory botanical, interrupts c-myc oncogenic signaling and synergizes with enzalutamide to induce apoptosis in prostate cancer cells *Mol Cancer Ther* 2016; 15(11):2791-2801. PMID: 27474149. Article Request Form

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The c-Myc gene encodes an oncoprotein transcription factor that is frequently upregulated in almost all cancer types and is the subject of intense investigation for management of cancer because of its pleiotropic effects controlling a

spectrum of cellular functions. However, due of its nonenzymatic nature, development of suitable strategies to block its protein-protein or protein-DNA interaction is challenging. Thus, c-Myc has been recognized as an elusive molecular target for cancer control, and various approaches are in development to inhibit c-Myc transcriptional activity. We observed that wedelolactone (WDL), an anti-inflammatory botanical compound, severely downregulates the expression of c-Myc mRNA in prostate cancer cells. Moreover, WDL dramatically decreases the protein level, nuclear accumulation, DNA-binding, and transcriptional activities of c-Myc. c-Myc is a transforming oncogene widely expressed in prostate cancer cells and is critical for maintaining their transformed phenotype. Interestingly, WDL was found to strongly affect the viability of Myc-activated prostate cancer cells and completely block their invasion as well as soft agar colony formation in vitro WDL was also found to downregulate c-Myc in vivo in nude mice xenografts. Moreover, WDL synergizes with enzalutamide to decrease the viability of androgen-sensitive prostate cancer cells via induction of apoptosis. These findings reveal a novel anticancer mechanism of the natural compound WDL, and suggest that the oncogenic function of c-Myc in prostate cancer cells can be effectively downregulated by WDL for the development of a new therapeutic strategy against Myc-driven prostate cancer. Mol Cancer Ther; 15(11); 2791-801. (c)2016 AACR.

Urology
Sarveswaran S, **Varma N**, **Morisetty S**, and **Ghosh J**. Inhibition of 5-lipoxygenase downregulates stemness and kills prostate cancer stem cells by triggering apoptosis via activation of c-Jun N-terminal kinase *Oncotarget* 2016;PMID: 27880719. Full Text

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The cancer stem cell (CSC) concept suggests that neoplastic clones are maintained exclusively by a rare group of cells possessed with stem cell properties. CSCs are characterized by features that include self-renewal, pluripotency and tumorigenicity, and are thought to be solely responsible for tumor recurrence and metastasis. A hierarchically organized CSC model is becoming increasingly evident for various types of cancer, including prostate cancer. The CD44 (+), CD133 (+) cell subpopulations were isolated from human prostate tumors which exhibit stem-like properties showing therapeutic-resistance, capacity of self-renewal, and exact recapitulation of the original tumor in vivo. Thus, an important challenge is to find measures to eliminate these cancer stem cells, which will stop tumor growth and prevent disease-recurrence. However, knowledge about molecular features critical for the survival of prostate cancer stem cells (PCSC) is meager. Here we report that inhibition of 5-lipoxygenase (5-Lox) by shRNA or MK591 dramatically kills PCSC by inducing apoptosis, suggesting that 5-Lox plays an essential role in the survival of PCSC. Interestingly, MK591 treatment decreases protein levels and inhibits transcriptional activities of Nanog and c-Myc. Since Nanog and c-Myc play important roles as stemness factors, our findings indicate that the 5-Lox activity plays a causal role in maintaining prostate cancer stemness via regulation of Nanog and c-Myc, and suggest that further exploration of 5-Lox-mediated signaling in PCSC may lead to development of novel, target-based, durable strategies to effectively block development and growth of prostate tumors, and prevent prostate cancer recurrence.

Urology
Seisen T, **Jindal T**, **Karabon P**, **Sood A**, Bellmunt J, Roupret M, Leow JJ, **Vetterlein MW**, Sun M, **Alanee S**, Choueiri TK, Trinh QD, **Menon M**, and **Abdollah F**. Efficacy of systemic chemotherapy plus radical nephroureterectomy for metastatic upper tract urothelial carcinoma *Eur Urol* 2016;PMID: 27912971. Full Text

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Given the growing body of evidence supporting the benefit of primary tumor control for a wide range of metastatic malignancies, we hypothesized that chemotherapy plus radical nephroureterectomy (RNU) is associated with an overall survival (OS) benefit compared to chemotherapy alone for metastatic upper tract urothelial carcinoma (mUTUC). Within the National Cancer Data Base (2004-2012), we identified 398 (38.4%) and 637 (61.6%) patients who received chemotherapy plus RNU and chemotherapy alone, respectively. Inverse probability of treatment weighting (IPTW)-adjusted Kaplan-Meier curves showed that 3-yr OS was 16.2% (95% confidence interval [CI] 12.1-20.3) for chemotherapy plus RNU and 6.4% (95%CI 4.1-8.7) for chemotherapy alone ($p<0.001$). In IPTW-adjusted

Cox regression analysis, chemotherapy plus RNU was associated with a significant OS benefit (hazard ratio 0.70, 95% CI 0.61-0.80; p<0.001). Despite the usual biases related to the observational study design, our findings show a net OS benefit for fit patients who received chemotherapy plus RNU for mUTUC relative to their counterparts treated with chemotherapy alone. PATIENT SUMMARY: We examined the role of radical nephroureterectomy in addition to systemic chemotherapy for metastatic upper tract urothelial carcinoma. We found that such treatment may be associated with an overall survival benefit compared to chemotherapy alone in fit patients.

Urology
Williamson SR, Eble JN, and **Palanisamy N**. Sclerosing TFEB rearrangement renal cell carcinoma: A recurring histologic pattern *Hum Pathol* 2016;PMID: 27864122. Full Text

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Renal cell carcinoma with TFEB rearrangement [t(6;11)(p21;q13)] was initially recognized to be composed of dual populations of large cells with clear cytoplasm and small cells forming rosettes around hyaline material. With increasing awareness, however, the spectrum of described morphology has been found to be more heterogeneous. We report a 54 year-old woman who underwent partial nephrectomy for a 2.4 cm renal mass, composed of fibrosis, hyalinization, calcification and ossification, and a smaller component of epithelioid cells. Immunohistochemical staining revealed diffuse positivity for cytokeratin AE1/AE3 and PAX8, patchy labeling for melan-A, HMB45, and cathepsin K, and negative caldesmon, SMA, TFE3 protein, carbonic anhydrase IX, CD10, CK7, EMA and inhibin. Fluorescence in situ hybridization confirmed rearrangement of TFEB and not TFE3. Together with one recent case in another report, our findings suggest that extensive sclerosis and ossification may be a less common recurring histology of TFEB rearrangement renal cell carcinoma.

Urology
Zaffuto E, Gazdovich S, Leyh-Bannurah SR, Huland H, **Abdollah F**, Shariat SF, **Menon M**, Briganti A, Montorsi F, and Karakiewicz PI. Contemporary rates of pathological features and mortality for adenocarcinoma of the urinary bladder in the USA *Int J Urol* 2016;PMID: 27875858. Full Text

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OBJECTIVES: To examine contemporary rates of pathological features and mortality for adenocarcinoma of the urinary bladder in the USA using population-based data analysis. METHODS: We relied on 10 024 patients with non-metastatic bladder cancer diagnosed between 2004 and 2013 within the Surveillance, Epidemiology and End Results registries. Logistic regression analyses focused on grade and stage. Kaplan-Meier analyses assessed cancer-specific mortality rates in adenocarcinoma and urothelial carcinoma of the bladder. Cox regression analyses assessed the impact of histological subtype on cancer-specific mortality. RESULTS: Overall, 215 (2.1%) adenocarcinoma and 9809 (97.9%) urothelial carcinoma patients were identified. The rate of non-organ-confined disease was higher in adenocarcinoma (64.7% vs 50.8%, P < 0.001). In multivariable logistic regression analyses, adenocarcinoma patients had a 2.2-fold higher risk of harboring non-organ-confined disease (95% confidence interval 1.7-3.0; P < 0.001) than urothelial carcinoma patients. Cancer-specific mortality-free survival rates were lower in adenocarcinoma (P < 0.01). This disadvantage only applied to non-organ-confined disease (P = 0.044), and not to organ-confined disease (P = 0.9). In multivariable Cox regression analyses, adenocarcinoma conferred a 1.3-fold higher rate of cancer-specific mortality (hazard ratio 1.30, 95% confidence interval 1.05-1.60; P = 0.01). Among adenocarcinoma patients, 30.7% harbored signet-ring cell adenocarcinoma and portended particularly poor cancer-specific mortality rates. CONCLUSIONS: In bladder cancer, adenocarcinoma presents at higher stages than urothelial carcinoma. However, cancer-specific mortality rates do not differ. A more unfavorable stage at diagnosis and higher cancer-specific mortality apply to the signet-ring cell variant.